

**EFFECT OF DIET AND ATMOSPHERE
ON INTESTINAL AND SKIN FLORA**

Vol. II - Literature Survey

by

**Phyllis E. Riely
Lorraine S. Gall, Ph.D.**

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INTRODUCTION

The microflora of the integument of the human body is composed of a varied population of differing microorganisms which may be influenced by the environmental factors to which the host is exposed as well as the particular personal hygienic procedures used by the host and which has never been completely defined on subjects living under the differing environmental conditions encountered in space flight, such as 100% oxygen atmosphere at reduced pressures, minimal personal hygiene care, and the wearing of a tight-fitting space suit.

As a basis for detecting the influence of such conditions of space flight on the skin flora and of understanding the possible effect of any changes induced, it is necessary to define as completely as possible the microflora present on the human integument under ordinary environmental conditions. The cornerstone of any such study is a comprehensive survey of the literature pertaining to this subject, to summarize and evaluate the existing knowledge so that areas in which information is deficient may be recognized and remedial action suggested. These are the goals of this report. This report considers the microflora of the integument to be those microorganisms which exist in or on the skin, but excluding those growing on mucous surfaces, and includes the following general and specialized skin areas; i. e., anal fold, axilla, external ear, eye, fingernails, scalp, toenails, and umbilicus. The microflora considered included both aerobic and anaerobic bacteria, yeasts, molds, fungi, actinomyces and viruses. Each reference was reviewed critically and evaluated on the following points:

- a. Whether the methods used offered valid information
- b. Whether the flora was truly indigenous
- c. Whether or not the subjects were healthy
- d. Whether the papers were published by recognized authorities

Those papers which most closely fulfilled the criteria set forth above were abstracted and will be discussed under review of the literature. Many other excellent papers were reviewed and considered worthy of inclusion in the report, although the material was not pertinent to the main objectives of this study and, for this reason, these papers will be found in the bibliography rather than in the reference section.

In addition pertinent observations made (during two contractual studies conducted by Republic Aviation Corporation personnel) on the microflora of the integument of men before, during and after being subjected to certain simulated space flight conditions will be included in this report as a basis for comment and comparison. These studies are "Research on Biomedical Criteria for Personal Hygiene" (AF33(615)-1814) and "Effect of Diet and Atmosphere on Intestinal and Skin Flora" (NAS 9-4172). The first study included a comprehensive microbiological survey of the skin flora from four groups of four men who were confined for thirty-three days and who were sampled in several skin areas thirteen times during that time period. These men, while living in a "closed" community, were under ambient atmospheric conditions in contrast to the men in the latter study who were under 100% oxygen at 5 psia for 20 days. In the latter study, six of the men were confined together under the test atmosphere, while two men, who served as controls, were confined at ambient atmospheres. The repeated sampling of these two groups of men before they were subjected to experimental conditions should substantially increase the knowledge of the "normal" skin flora. Experimental conditions common to both contractual studies were the use of minimal hygiene procedures which excluded bathing by all the subjects and the superimposition of certain periods of wearing space suits by some of the subjects. The data from the portions of the experiment when simulated space flight conditions prevailed will be considered separately.

REVIEW OF LITERATURE

Normal Bacterial Skin Flora - General

One of the first meaningful studies designed to define the flora of the "normal" skin was made by Price (1938)⁽¹⁾. This careful work was based on a modified scrubbing procedure and included a sampling of the rinse water from the hands and forearms. The value of this particular study was impaired by the use of soap in the scrubbing procedure, which probably explains the lack of recovery of the common diphtheroids of the skin. For this reason the counts as reported in Price are essentially those of micrococci. His original concept that the transient flora of the skin was on the surface and would be recovered in the first rinse while the native flora was deeper in the skin and would be found in the following rinse is not necessarily valid as a recent paper of Rebell (1962)⁽²⁾ points out that "if the skin is reasonably clean, however, recovery of exogenous bacteria and mold spores closely follows that of endogenous bacteria", because the indigenous flora actually is superficial and will be removed in the initial wash.

Rebell⁽²⁾ in agreement with most authors found that the bacterial counts in different areas of the body differed widely. "Areas rich in sebaceous glands and, more especially, intertriginous areas support a much larger population of bacteria than does the general body surface." "If the skin remains unwashed, bacterial counts from intertriginous sites increase proportionately more than those from the body surface generally, and may exceed 100,000,000 micrococci per sq. cm." The following skin micrococci were identified in this study: Micrococcus epidermidis, Micrococcus aurantiacus and Micrococcus candidus and a small number of Micrococcus flavus. Rebell states that "Staphylococcus pyogenes is not a permanent member of the normal skin flora, although it may become established in this flora for short periods."

Rebell⁽²⁾ considers that one of the most abundant microorganisms on the skin is the diphtheroids, but since they require oleic acid for growth, at times, their recovery is difficult. They are most numerous in the intertriginous regions where they may exceed 1,000,000 per sq. cm, while this author did not find them in the scalp or the exposed skin areas. He mentions the presence of Corynebacterium acne in the depths of the sebaceous follicles of the face, chest, and back. "High counts of the acne bacillus reported from the total skin are almost certainly due to confusion with oleic acid requiring diphtheroids of the skin surface. The diphtheroids of the skin fall roughly into groups: lipophilic aerobes, lipophilic anaerobes, and lipid independent forms including the erythrasma bacillus, Corynebacterium minutissimum."

One of the most comprehensive surveys of the literature with regard to the indigenous skin flora was compiled by Rosebury (1962)⁽³⁾, who lists the normal indigenous microflora of the skin as follows: coagulase-negative staphylococci, aerobic corynebacteria, C. acnes, occasionally mycobacteria, and Candida albicans as well as other candidas, Pityrosporum ovale, P. orbiculare. The values given by Rosebury for skin are based on the work of several authors, including Price (1938)⁽¹⁾ and Evans (1950)⁽⁴⁾ and Pachtman, Vicher, and Brunner (1954)⁽⁵⁾. All of these studies were comprehensive and yielded valuable information in the area of the authors' interest. In addition to the bacteria found on the skin, Rosebury⁽³⁾ reviewed the work of authors who stress the importance of varying species of fungus. The species as reported by Rosebury were Candida albicans, other candidas, Torulopsis glabrata, Pityrosporum ovale, P. Orbiculare, Dermatophytes and reflect the work of Benham and Hopkins (1933)*, Croft and Black (1938)**, Emmons (1940)***, Gordon (1951)****, and DiMenna (1954)*****.

* Benham, R.W.; and Hopkins, A. Mch.: Arch. Dermatol. Syphilol., vol 28, 1933, pp. 532.

** Croft, C.C.; and Black, L.A.: J. Lab. Clin. Med., vol. 23, 1938, pp. 1259.

*** Emmons, C.W.: Public Health Repts., vol. 53, 1938, pp. 1967.

**** Gordon, M.A.: J. Invest. Dermat., vol. 17, 1951, pp. 267.
Gordon, M.A.: Mycologia, vol. 43, 1951, pp. 524.

***** DiMenna, M.E.: J. Path. Bacteriol., vol. 68, 1954, pp. 89.

The data collected by Rosebury⁽³⁾ from his review of the literature and from his own studies are summarized in his text in a table pertinent areas of which are presented in full in this report in Table 1.

Rosebury's⁽³⁾ book fills a significant need as it has highlighted many areas that need investigation before the normal indigenous flora of man can truly be defined. He emphasizes the important part that the normal flora undoubtedly plays since, "Whenever a given microbic species is found regularly and in appreciable numbers in an indigenous locus, it may be assumed that its metabolic activity directly or indirectly influences the host...".⁽³⁾

Rosebury's⁽³⁾ book has been followed by "The Ecology of the Human Skin" by Mary Marples (1963)⁽⁶⁾, who in her exhaustive study of the ecology of the human skin has considered many factors, i.e., environment, physiology, genetic as well as the varied inter-reactions between all of these factors.

A thorough understanding of the environment of the cutaneous flora is essential and M. Marples⁽⁶⁾ felt that "The general surface consisting of a substrate of fully keratinized desquamating epidermal fragments, which is bathed with sweat and sebaceous secretion..." is an environment which will be modified by any radical change in heat or moisture. In addition there are: superficial structures, which are hard keratin such as hair or nails; epidermal invaginations; deeper layers of the epidermis; and the dermis.

Marples⁽⁶⁾ is cognizant of the immense variation in the number of organisms isolated from the skin of the same individual at different times and realizes that the individual variation includes the ability to support a larger and denser bacterial population. This cutaneous population is only temporarily affected by sweating or washing. She summarizes admirably the work of many authors which have been reviewed in this report individually and therefore will not be included at this point in the text.

Marples⁽⁶⁾ also summarizes the normal flora of the skin in her text, which is included in part in this report in Table 2. Her data differs slightly from that of Rosebury⁽³⁾, but there is general agreement between the two reviews.

Table 1

"MICROORGANISMS COMMONLY FOUND ON HEALTHY HUMAN BODY SURFACES"^a

Species or group	Skin			
	General	Feet	External auditory canal	Conjunctiva
A. Gram-positive cocci: Coagulase-negative staphylococci	88-100 2-6/cm ²		27-100	37-94
Coagulase-positive staphylococci	5-24		12-20	0-30
Anaerobic micrococci	±			
<u>Str. mitis</u> and undifferentiated α and γ streptococci	±0		0.2-23	0.9-1
<u>Str. hominis</u> (salivarius)				
Enterococci or group D strepto- cocci				
<u>Str. pyogenes</u> (usually group A unless noted)	0-4			0.3-2.5
Anaerobic streptococci				
<u>D. pneumoniae</u>			+	0-5
B. Gram-negative cocci: <u>N. catarrhalis</u> and other spp.				
<u>N. meningitidis</u>				
<u>V. alcalescens</u>				2.3
C. Gram-positive bacilli: Lactobacilli				

^a Rosebury (1962)⁽³⁾

Table 1 (cont.)

MICROORGANISMS COMMONLY FOUND ON HEALTHY HUMAN BODY SURFACES^a

Species or group	Skin			
	General	Feet	External auditory canal	Conjunctiva
Aerobic corynebacteria	53		86	3-83
<u>C. acnes</u>	5/cm ²			
Mycobacteria	45-100			
<u>Cl. perfringens</u> , other spp.	6/cm ²			
<u>Cl. tetani</u>	+			
<u>Actinomyces bifidus</u>				
<u>A. israelii</u>				
<u>Leptotrichia buccalis</u>				
<u>L. dentium</u>				
D. Aerobic Gram-negative bacilli:				
Undifferentiated "coliforms"			4-8	2.1
<u>Escherichia coli</u>			0.1-0.4	
"Intermediates"			+	0.1
<u>Klebsiella aerogenes</u>			0.2-1	0.4
<u>Proteus mirabilis</u> , other spp.			0-1.3	
<u>Pseudomonas aeruginosa</u>			1.1-1.6	±
<u>Alcaligenes faecalis</u>				
<u>Vibrio alcaligenes</u>				±
<u>Moraxella lacunata</u>				±
<u>Mima polymorpha</u>				

^a Rosebury (1962)⁽³⁾

Table 1 (cont.)

MICROORGANISMS COMMONLY FOUND ON HEALTHY HUMAN BODY SURFACES^a

Species or group	Skin			
	General	Feet	External auditory canal	Conjunctiva
<u>M. vaginalis</u>				±
<u>Haemophilus influenzae</u>				0.4-2.5
<u>H. parainfluenzae</u>				
<u>Hemolytic hemophili</u>				+
<u>H. aegyptius</u>				
<u>H. vaginalis</u>				
F.				
<u>Candida albicans</u>	±	±	+	
Other candidas	1-15	+	+	
<u>Torulopsis glabrata</u>				
<u>Pityrosporum ovale</u>	100			
<u>P. orbiculare</u>	++			
Dermatophytes		2-41		

^a Rosebury (1962)⁽³⁾

Table 1 (cont.)

MICROORGANISMS COMMONLY FOUND ON HEALTHY HUMAN BODY SURFACES^a

Species or group	Skin			
	General	Feet	External auditory canal	Conjunctiva
A. Gram-positive cocci: Coagulase-negative staphylococci Coagulase-positive staphylococci	88-100		27-100	37-94

± 0, rare±, irregular or uncertain

+, common

++, prominent

Numbers = range of incidence in percent

Values given with units = range of concentrations expressed as lag₁₀*^a Rosebury (1962)⁽³⁾

Table 2

DISTRIBUTION OF MICRO-ORGANISMS IN VARIOUS CUTANEOUS HABITATS ^a

Habitat	Residents	Frequent visitors	Rare visitors
Surface of skin	<u>Pediculus humanus</u> <u>Pityrosporum ovale</u> Non-pigmented yeasts <u>Staph. epidermidis</u> <u>Micrococcus</u> spp. <u>Corynebacterium</u> spp. <u>Mycobacterium smegmatis</u> <u>Treponema</u> spp.	<u>Pulex irritans</u> <u>Staph. aureus</u> Gram negative bacilli Aerobic spore-formers	<u>Aspergillus</u> spp. <u>Candida albicans</u> <u>Streptococcus</u> spp. <u>Neisseria</u> spp.
Layers of stratum corneum	<u>Staph. epidermidis</u> <u>Micrococcus</u> spp. <u>Corynebacterium</u> spp.	<u>Sarcoptes scabiei</u> Dermatophytes <u>Staph. aureus</u> <u>Strep. pyogenes</u>	various mites <u>Entamoeba histolytica</u> <u>Cladosporium wernecki</u> <u>Pityrosporum orbiculare</u> <u>Candida albicans</u> <u>Mycobacterium balnei</u> <u>B. anthracis</u> <u>C. diphtheriae</u> <u>Pasteurella</u> spp.
Malpighian layers of the epidermis	<u>Herpesvirus hominis</u>	<u>Treponema pertenue</u> papova virus VZ. virus	Larval helminths <u>Mycobacterium</u> spp. <u>Treponema carateum</u> <u>Poxvirus variolae</u> and other spp.
Pilosebaceous unit	<u>Demodex folliculorum</u> <u>Pityrosporum ovale</u> <u>Corynebacterium acnes</u> <u>Aerobic corynebacteria</u>	<u>Trichophyton</u> spp. <u>Microsporum</u> spp. <u>Staph. aureus</u>	<u>Microsporum gypseum</u> <u>Piedra</u> spp. <u>Corynebacterium tenuis</u>
Eccrine sweat gland	-	<u>Staph. epidermidis</u> <u>Staph. aureus</u>	<u>Pasteurella pestis</u> Chromogenic bacteria

^a Marples (1965) ⁽⁶⁾

Table 2 (cont.)

DISTRIBUTION OF MICRO-ORGANISMS IN VARIOUS CUTANEOUS HABITATS ^a

Habitat	Residents	Frequent visitors	Rare visitors
Dermis	-	<u>Leishmania spp.</u> <u>Mycobacterium leprae</u>	<u>Dracunculus medinensis</u> <u>Larval helminths</u> <u>Cladosporium spp.</u> <u>Nocardia spp.</u> <u>Mycobacterium spp.</u>

^a Marples (1965)⁽⁶⁾

In her discussion of the normal flora, Miss Marples⁽⁶⁾ feels that the predominant aerobic organisms on the skin of the adult are gram-positive coagulase-negative cocci, and diphtheroids.

The diphtheroid members of the skin flora include both aerobic and anaerobic forms. The literature seems to contain a predominant amount of evidence for the prevalence of the anaerobic diphtheroid known as Corynebacterium acnes or Propionibacterium acnes. "In adult subjects Corynebacterium acnes appears to be a dominant member of the cutaneous community." "Aerobic diphtheroids are numerous and varied. They must be important in the ecology of the human skin and they deserve more attention than they have hitherto received:"...⁽⁶⁾

The two texts by Rosebury⁽³⁾ and Marples⁽⁶⁾ are excellent and complement each other in the critical area of normal flora of the skin. Rosebury with his tables of the normal flora has been of inestimable help to microbiologists, and he has also defined many problem areas where sufficient data are not available. If only one book could be purchased on normal skin microflora, Rosebury⁽³⁾ would seem best for the microbiologist and Mary Marples "Ecology of the Human Skin"⁽⁶⁾ for a physician or physiologist, since in her book the areas dealing with fungus infection and tropical skin diseases are particularly good, and Marple's⁽⁶⁾ text also covers a much wider area than Rosebury's⁽³⁾, although it is not as specific in certain instances.

Additional confirmation of the work of other authors on the normal skin flora was added by the work of Fritsch and Fritsch (1964)⁽⁷⁾ who differentiated between the resident and transient flora and list the resident flora as consisting of micrococcus, corynebacteria, propionibacterium and pityrosporum. The transient flora includes micrococcus, streptococcus, gram-negative rods, gram positive spore-formers, Candida and cryptococcus.

"In contrast to the transient flora of the skin with its highly variable composition (reflecting the changing bacterial environment), the resident flora is found to consist of very large numbers of some half-a-dozen species of bacteria. Though the number and distribution of these different organisms is

affected to some extent by such variables as the climate, and the age, hygiene, clothing and general activities of the individual and differs greatly from one anatomical site to another. The resident flora as a whole can be regarded as a mixed population of a few species of saprophytic bacteria in equilibrium with their immediate environment. "(8) Gleeson-White (1960)⁽⁸⁾ recovered most of the aerobes from the intertriginous zones including the sebaceous skin of the face, scalp and upper chest. The poorest recovery was from the non-hairy skin of the trunk. If a count of the anaerobes present is included, a direct relationship exists between the distribution of the resident flora and the sebaceous glands. The following types of bacteria were recovered: aerobic gram positive cocci, diphtheroid bacilli, Micrococcus candidus, Micrococcus flavus; the principle aerobe was Staphylococcus albus while the principle anaerobe was the acne bacillus.

Allende⁽⁹⁾ studied the normal flora of the limbs in an attempt to clarify infection as it appears on the stumps of amputees. As reported in this study, the normal skin contained the following number of colonies located on the control limb:

Table 3
NORMAL FLORA OF THE LIMBS

"Subject	Albus	Diphtheroids	Sarcina	E. coli	Anaerobic Staph	Anaerobic Diphtheroids	Gram Positive Rod
1	150	125	175	25	--	--	--
2	100	--	--	--	--	--	--
3	725	125	--	--	875	200	--
4	150	--	--	--	400	--	--
5	--	--	--	--	--	--	--
6	50	--	50	--	50	--	50
7	--	--	--	--	--	--	--
8	--	--	--	--	--	--	(rare)
9	200	200	--	--	--	--	--
10	--	--	--	--	--	--	-- "

These counts emphasize the marked individual variation present in the normal population.

Updegraff (1964)⁽¹⁰⁾ characterized the normal skin flora as cocci, and occasional bacilli which were of three types: long slender rods, short thick rods, and an intermediate type (they were probably diphtheroids). He considered the resident flora to include Corynebacterium acnes, Staphylococcus epidermidis, and aerobic diphtheroids which gave total counts of 6 to 865,000 per/cm². The anaerobes outnumbered the aerobes from 10 to 100 fold. These findings were at variance with some authors and Updegraff attributed these differences to the sampling technique. Accordingly he conducted a careful study on the technique of sampling which led to his method of using scotch tape in the Wolf tradition and which was found to be non-inhibitory if Scotch brand 850 industrial tape was used. Three to five strippings were removed from the test areas, placed face up in Petri dishes and covered with agar. Counts were made on the second and fourth strippings of the backs of 13 men. One strip was incubated aerobically, the other anaerobically. Wide variation was found among individuals from zero to more than 300 colonies per 4 cms². With one exception, aerobic and anaerobic counts agreed very well. All colonies on the tapes were small, circular, and white.

From the review of the literature, it is apparent that staphylococci and diphtheroids are the most prevalent skin microorganisms. Because the literature on staphylococci is so voluminous and is closely tied in with several frankly pathogenic skin conditions, the papers on staphylococci will be reviewed later in this report. However, the work of several authors who have devoted their research to a study of the diphtheroids occurring on the human skin will be discussed here.

Pollack, et al: (1946)⁽¹¹⁾ isolated 52 diphtheroid strains from the human skin, five of which were oleic acid requiring. These lipophilic diphtheroids have been identified as Corynebacterium xerosis by Pillsbury and Kligman (1954)⁽¹²⁾. Marples and Bailey (1957)⁽¹³⁾ also found diphtheroids in the interdigital skin of the foot in 38.2 percent of 175 adult subjects. "Aerobic diphtheroids do not appear to produce any overt changes in the skin and must be regarded as normal residence of the substrate."⁽¹³⁾

Four papers which support the presence of the streptococci on normal skin of some individuals are reviewed.

Among other important contributions to the definition of the normal flora have been those of Rebell (1947)⁽¹⁴⁾ who highlighted the appearance of hemolytic streptococci in a significant portion of his subjects in addition to the flora recovered by other authors.

In a small series of children (8) streptococci were isolated by Evans (1950)⁽⁴⁾ from the skin of six. Perhaps enough variation in pH of the skin exists between children and adult to allow the survival of streptococci. Perhaps this also occurs in the cutaneous infections of erysipelas and impetigo where streptococci multiply very rapidly in the superficial layers of the skin, and it is interesting to wonder about the pH of these particular skins. However, Price (1938)⁽¹⁾ reported that while he was attending patients with streptococcal wound infections, it was possible to isolate streptococci among the normal flora of his hands and forearms.

In Cook Islands, Markham and Stenhouse (1959)⁽¹⁵⁾ were able to isolate streptococcus pyogenes from 81% of impetiginous lesions, and in addition streptococcal strains were recovered from 13% of 48 samples of normal skin. They also recovered toxigenic strains of Corynebacterium diphtheria from 40% of lesions of impetigo and only once from normal skin.

The recovery of Mycobacterium smegmatis by Cruickshank and Cruickshank (1931)⁽¹⁶⁾ adds another candidate for the list of the normal flora.

Mycobacterium smegmatis is one of the normal inhabitants of the skin living in the particular location of the external genitalia. Its function has never been clearly defined and pathogenicity does not seem to be related to its presence in that locality. Other mycobacteria of the group IV have been found in varied localities in the skin but have never been given truly indigenous status. Of particular interest is the sensitivity developing from exposure to mycobacteria since as is shown by Edwards and Palmer (1959)⁽¹⁷⁾ more than 60% of Navy recruits in Georgia and Florida have been previously sensitized to mycobacteria. The other members of the Mycobacteriaceae are pathogenic in relation to the position on the integument.

One of the species of mycobacterium M. leprae does establish itself on the skin of contacts living in close proximity to a patient with active leprosy. Whether its presence is truly indigenous is a moot point.

According to Marples⁽⁶⁾, two treponemes are considered to be members of the normal flora of the skin of the genitalia. These are T. calligyrum and T. genitalis. These species do not seem to be associated with any form of lesion on the human skin and it is possible that they are transients derived from the anorectal mucosa. The other members of the treponemes are usually associated with the venereal disease and include the organisms which cause syphilis, yaws and pinta.

The early work of Meyer (1932)⁽¹⁸⁾ confirmed the work of other authors, but added Sarcina lutea and certain gram negative rods to the "growing" flora of the skin.

Miscellaneous bacterial inhabitants of the skin include Mima polymorpha as well as neisseria and perhaps Streptomyces coelicolor (Heynier, 1957⁽¹⁹⁾). PPLO organisms also have been isolated from 3.3% of 150 subjects cultured by Melczar and Vasarkelyi (1959)⁽²⁰⁾.

One of the few studies in which subjects were placed under certain conditions similar to space flight was conducted by Christie⁽²¹⁾ in which men were isolated from additional contacts and in which minimal personal hygiene was practiced. Isolated arctic scientists were cultured to discover whether their flora would remain the same or would have a tendency to become more like that of their fellow scientists. These men were maintained on a Greenland ice cap for 100 days and two had no contact with soap and water. Others of the men did not wash for 5-7 days and showed no significant increase in the total number of bacteria. The flora seemed to simplify as time elapsed. In the beginning, the following organisms Staphylococcus albus, Staphylococcus aureus, Neisseria catarrhalis, diphtheroids, Bacillus subtilis and Gaffkya tetragena were recovered. After the 100 days of isolation, Bacillus subtilis seemed to become predominant and the secondary organism was Staphylococcus albus with Staphylococcus aureus occurring in two of the scientists.

Other studies are in progress to establish the effect of certain simulated space conditions including isolation, wearing space suits, minimal personal hygiene procedures and 100% oxygen at altitude on the indigenous flora of man. To establish a baseline of the truly indigenous flora, repeated cultures of the same individuals for many varied body areas using both aerobic and anaerobic techniques (in different seasons of the year) is necessary and two current studies^(22, 23) at Republic Aviation Corporation considering this factor should add substantial data to the normal flora.

The purpose of one of these studies⁽²²⁾ is to obtain hygienic and microbiological data pertaining to the indigenous microflora of the human and his surrounding environment under controlled conditions simulating space travel and to use the information derived from this study to establish biomedical criteria for personal hygiene and sanitation for long-term aerospace missions as well as to provide indices of deterioration of environmental condition.

From the extensive microbiological procedures performed, data has been extracted which is pertinent to this determination of the normal skin flora. It is necessary to realize that minimal personal hygiene procedures were in force throughout the study. The subjects showered before entry into the evaluator and during their stay only "wet wipes" were allowed and were limited to three a day for hand wiping following eating and defecation. It is possible that the height of the colony count from certain body areas is a reflection of the minimal personal hygiene procedures. However, the body areas are not radically different in a qualitative analysis of the kinds of bacteria present although the quantitative data presented must be evaluated.

Four different groups of subjects of four men each have spent periods of approximately 42 days in a confined environment with all contacts strictly limited and with the use of surgical garments and masks by the contacts in order to prevent cross contamination. The data is summarized by subjects and Table 4 illustrates the relationship between staphylococcus and corynebacteria at varying sampling periods from varying body areas on subjects 29, 30, 31, and 32.

The bacteria recovered from varied body areas are shown in table format under specialized body areas.

Table 4

INCIDENCE OF CORYNEBACTERIA AND STAPHYLOCOCCI IN SELECTED BODY AREAS^a

DURING VARIOUS SAMPLING PERIODS

Sampling Period

Area Subj.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Ear (29)																
Coryn.	-	120	310	60	120	-	-	-	-	20	-	-	-	-	-	-
Staph.	1500	200	70	70	110	780	70	440	830	440	79	660	6	77	180	360
Ear (30)																
Coryn.	0	0	0	4	0	0	0	0	0		0	0	0	0	200	3
Staph.	0	1	0	0	0	0	0	2	1	0	1	50	3	7	30	7
Ear (31)																
Coryn.	5000	600	550	3000	5000	600	4500	5500	5500	880	200	-	-	-	30	-
Staph.	20	13	15	200	20	30	20	50	90	2940	70	73	380	1500	20	1340
Ear (32)																
Coryn.	170	-	400	214	120	1200	15	30	-	69	-	-	2	-	-	-
Staph.	36	610	73	200	150	40	7	110	3	65	15	53	110	670	110	2600

Data equivalent to 10^{-4} total bacteria per gram of sample

Coryn. = Corynebacterium sp

Staph. = Staphylococcal sp

a Biomedical Criteria (AF33(615)-1814⁽²²⁾)

b No Sample

Table 4 (cont.)

INCIDENCE OF CORYNEBACTERIA AND STAPHYLOCOCCI IN SELECTED BODY AREAS^a

DURING VARIOUS SAMPLING PERIODS

Area Subj.	Sampling Period															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Toes (29)	Coryn.	3500													50000	9000
	Staph.	1900							NS ^b						30000	13100
Toes (30)	Coryn.	5250							26200							2000
	Staph.	2000							4200							3900
Toes (31)	Coryn.	6000							5500						70000	20000
	Staph.	2500							3200						70000	40000
Toes (32)	Coryn.	165					12000									32500
	Staph.	83														4300

Data equivalent to 10^{-4} total bacteria per gram of sample.Coryn. = *Corynebacterium* spStaph. = *Staphylococcus* sp^a Biomedical Criteria (AF33(615)-1814⁽²²⁾)^b No Sample

Table 4 (cont.)

INCIDENCE OF CORYNEBACTERIA AND STAPHYLOCOCCI IN SELECTED BODY AREAS^a
DURING VARIOUS SAMPLING PERIODS

Area Subj.		Sampling Period															
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Axilla (29)	Coryn.	250	5000	-	5000	5200	2000	900	5000	3500	5500	3000	150	5000	2000	4500	2000
	Staph.	75	30	1	160	220	520	240	920	280	340	350	980	490	140	730	1500
Axilla (30)	Coryn.	2000	2000	0	770	1750	2300	65	130	6000	2750	2800	0	2800	3000	TNTC	1000
	Staph.	220	1620	5	1020	1250	1450	15	51	1060	130	1160	3500	5700	1400	180	700
Axilla (31)	Coryn.	250	1020	11	100	500	40	5000	2560	1920	2120	1980	-	2410	80	-	2200
	Staph.	380	2020	116	400	1320	800	4800	3000	1150	1410	2400	2000	2500	1700	4850	550
Axilla (32)	Coryn.	-	-	-	40	900	800	1200	2000	1110	2750	3000	2000	3800	1900	TNTC	4500
	Staph.	48	1410	5	180	3620	5600	1600	860	550	2000	400	4800	2040	1400	4500	740

Data equivalent to 10^{-4} total bacteria per gram of sample

Coryn. = Corynebacterium sp

Staph. = Staphylococcal sp

^a Biomedical Criteria (AF33(615)-1814⁽²²⁾)

^b No Sample

Table 5

NORMAL SKIN FLORA BY AREA, AND AUTHOR

NOTE: Authors keyed by number - see list at end of table

	General Skin Area	Anal fold	Axilla	Ear	Eye	Fingernails	Scalp	Toenails - interdigital areas	Umbilicus
<u>Staph. aureus</u>	2, 5, 11		14	3, 15, 17	3, 18, 19		21		
Neisseria	11, 22	22	22	22	3, 18, 22		22		
Mima polymorpha			22	22	3				
PPLO		22	22						
Treponema		8							
Aerobacter <u>aerogenes</u>	22	22	2, 13, 22	17	18, 22	20			
D. Pneumoniae				3	3				
Coliforms	7	22		3, 15	3, 18	20			
E. Coli	5	22		3	18, 22			22	
Klebsiella				3	3				
Proteus				3, 15, 17	3, 18	20			
Pseudomonas				3, 15	18	20		22	

Table 5 (cont.)

NORMAL SKIN FLORA BY AREA, AND AUTHOR

NOTE: Authors keyed by number - see list at end of table

	General Skin Area	Anal fold	Axilla	Ear	Eye	Fingernails	Scalp	Toenails - interdigital areas	Umbilicus
<u>Staphylococci</u> albus	1, 22	22	2, 22	3, 15, 17, 22	3, 18, 19, 22		21	22	22
Aerobic <u>Corynebacterium</u>	2, 3, 5, 6, 9, 11, 22	2, 22	2, 13, 22	3, 15, 17, 22	3, 18, 19, 22	20	21, 22	2, 8, 22	22
<u>Pityrosporum</u> ovale	3			15			21, 3, 8, 16		
<u>Micrococci</u>	2, 9, 22	22	22	22	22	20	21, 22	22	22
<u>Streptococci</u>	2, 10	22	22	3, 15, 17	3, 18, 19, 22	20			22
<u>Sarcina</u>	5, 7	22	22	22	18	20			
<u>Gaffya</u>	11, 22		22						
<u>Corynebact.</u> acnes	3, 5, 6, 9, 22								
<u>Mycobacteria</u>	3, 4	22							
<u>Clostridium</u>		12, 22							
<u>Candida</u>	3	22		3, 22	18	20			

Table 5 (cont.)

NORMAL SKIN FLORA BY AREA, AND AUTHOR

NOTE: Authors keyed by number - see list at end of table

	General Skin Area	Anal fold	Axilla	Ear	Eye	Fingernails	Scalp	Toenails- interdigital areas	Umbilicus
<i>Alcaligenes faecalis</i>		22	13	3, 15	3				
<i>Moraxella lacunata</i>	22				3, 22				
<i>Haemophilus</i>					3				
Bacillaceae	11	22		17, 22	18		22	22	22
<i>Staph. citreus</i>				15	18				
<i>Pneumococcus</i>					18, 19				
Pro-actinomyces	22	22	22	22	22		22	22	22

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21. MacKee, George M.; and Lewis, George M.: (1938)
22. Republic Aviation Corporation: Contracts - AF33(615)-1814 and NAS 9-4172

A corollary study⁽²³⁾ on eight men, six of whom were under a high oxygen environment, was performed at the Naval Crew Equipment Laboratory in Philadelphia and this study gives some insight into the effect of oxygen at altitude, the wearing of space suits and minimal personal hygiene procedures on the skin flora, as well as additional data on the normal flora in certain skin areas. The results of the microbiological tests were interesting as the total colony counts from the axilla and groin increased as the experiment progressed; however, by mid-point in the experiment the counts seemed to plateau and remain relatively stable. The bacteria involved in the build-up of microflora in the axilla and groin were staphylococci or micrococci and Corynebacterium species. The build-up of corynebacteria in most instances represented a relative increase of the rod over the cocci. This build-up was most marked in the body areas where sweat is a factor and this pattern appeared to be the result of the minimal personal hygiene procedures on men in a confined environment. There was no marked difference in the microflora of the subjects during the period of 100% oxygen at 5 psia for 20 days or in the wearing of the space suit for three weeks.

Summary

The divergence of opinions of varied authors on the indigenous microflora seems to be a reflection of their sampling and cultural techniques. For this reason Table 5 has been compiled giving the flora of the various areas as determined by differing authors. Each author whose work is used in the table is numerically keyed and identified at the end of the chart.

One of the major areas of disagreement is in the presence or absence of Corynebacterium acnes which is dependent on cultural techniques as well as the depth from which the samples were secured. Another example of the importance of cultural technique is in the recovery of P. ovale as an oil overlay of the slant seems essential for their growth.

When the present knowledge is implemented by detailed studies performed under the same conditions of collection and culture it will be possible to truly define the indigenous biota of man.

SPECIALIZED SKIN FLORA

The biota of the general skin areas has been reviewed and since certain specialized areas support a slightly different flora, due to their own individual characteristics, they warrant separate consideration. The scalp, in many individuals, has an extensive hair covering, at least for certain periods of their life: The ear has a specialized secretion, cerumen, and its flora is rarely, if ever, disturbed by washing: The axilla differs from other body areas in several respects as this area has a number of apocrine glands, is often shaved, or is hair covered and in many individuals has anti-perspirants frequently applied: The anal folds are prone to contamination with fecal bacteria and other fecal matter which provides a heavy bacterial inoculum and appropriate nutrients: An ideal area for bacteria to live and thrive is under the fingernails: The interdigital webs or toenail areas offer fungus a chance to thrive since the area is often covered by clothing and perspiration offers sufficient growth material: The eye seems to come equipped with its own anti-bacterial secretions, yet many bacteria may grow there.

Anal Fold Microflora

One of the few articles that discusses the flora of the anal folds was that of Price and Shooter (1964)⁽²⁴⁾ who isolated Clostridium welchii from the anal folds and frequently from the skin some distance away. These commensal strains varied widely in their ability to form toxin, which raises the question whether their habitat influenced the toxin production.

The Republic Aviation Corporation study⁽²²⁾ also considered the anal folds as a specialized area since the possibility of fecal contamination is extremely high, particularly under the experimental conditions imposed in these trials. The findings of this study are extremely interesting and the bacteria present are summarized in Table 6. Both facultative and obligate anaerobes were found, many of which were typical fecal bacteria. This work is still in progress and more complete results will be found in the final report.

Table 6

OCCURRENCES OF VARIOUS MICROORGANISMS ON ANAL FOLD^a

Subject Number	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
<u>Micro-flora</u>																	
<u>E. coli</u>		x	x	x		x	x		x						x		
<u>Aerobacter</u>				x		x											
<u>Alk. dispar</u>						x									x		
<u>PPLO</u>	x	x	x	x					x	x			x	x			
<u>Streptococci</u>			x	x	x	x	x	x	x	x	x	x	(Work in progress)		
<u>Corynebacteria</u>	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x	
<u>Micrococci</u>	x		x														
<u>Clostridium</u>					x												
<u>Alcaligenes</u>				x													
<u>Lactobacillus</u>							x	x									
<u>Bacillaceae</u>		x				x	x	x									
<u>Proactinomyces</u>				x	x		x	x									
<u>Neisseria</u>											x						
<u>Anaerobes</u>	x	x	x	x													
<u>Staphylococcus</u>	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
<u>Obligate anaerobe</u>	x	x	x	x	(Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress)
<u>Fac. anaerobes</u>	x	x	x	x	(Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress	Work in progress)
<u>Candida</u>					x												
<u>Trichosporium</u>							x			x	x						
<u>Sarcina</u>	x	x													x		
<u>Scopulariopsis sp.</u>									x			x					
^a Biomedical Criteria (AF33(615)-1814). ⁽²²⁾																	

The fact that E. coli was not always recovered may be an important consideration since staphylococcus, streptococcus, and corynebacterium were recovered in the great majority of tests, and it is felt that these types of bacteria may represent the true predominating flora of the anal folds.

Axillary Microflora

"A knowledge of the organisms which normally inhabit the axilla is very scanty owing to lack of systematic study" according to Shehadeh, et al⁽²⁵⁾. These authors performed a thorough study to implement the knowledge of the bacterial flora of the axilla, and they differentiated between the resident and transient flora.

Table 7

'NORMAL AXILLARY FLORA

<u>Resident Flora</u>	<u>Number</u>	<u>Percent</u>
Coagulase negative staphylococci	49	98
Diphtheroids	38	76
Gram negative aerobacter	22	44
<u>Alkaligenes fecalis</u>	16	32
<u>Transient Flora</u>	<u>Number</u>	<u>Percent</u>
Sarcina	7	14
<u>Staphylococci aureus</u>	4	8
<u>Proteus vulgaris</u>	5	10
<u>E. coli</u>	3	6 " (25)

In many hundreds of axillary cultures, they⁽²⁵⁾ never isolated a culture displaying strict anaerobiosis. The authors felt that the resident corynebacteria are facultative. This finding is extremely important since many of the earlier authors neglected to establish the degree of anaerobiosis of their cultures and unless the oxidation-reduction potential of the medium has been established, the true anaerobiosis of the culture is in question. They⁽²⁵⁾ were unable to confirm the finding of

Shelley, et al: (1953)⁽²⁶⁾ that Staphylococcus aureus occurred in 8% of his subjects. The successive axillary counts obtained by these authors⁽²⁵⁾ is a valuable contribution to knowledge of the axillary flora. (Table 8)

Rebell⁽²⁾ recovered large numbers of diphtheroids from the axilla as well as the standard micrococcal flora and felt that Aerobacter aerogenes played an important role in many instances.

Republic Aviation Corporation's study⁽²³⁾ found the normal axillary flora to consist of corynebacteria, varied staphylococci, micrococcus, occasional sarcina, aerobacter, E. coli, and actinomyces. (Table 9)

The other similar Republic Aviation Corporation study⁽²²⁾ is in general agreement with these findings, as is shown in Table 10, and the axillary counts obtained in study⁽²²⁾ are summarized in Table 11.

Since topical application of antibacterial substances to the region of the axilla is a cultural requirement in many strata of society, a consideration of the effects of this application on the resident flora of the axilla is important. A detailed study was made by Kligman and Shehadeh (1963)⁽²⁷⁾. They considered the dominant resident flora to consist of coagulase-negative staphylococci, diphtheroids, Aerobacter sp and alkaligenes. Staphylococcus aureus appeared transiently. Five agents including several antibiotics alone or in combination with aluminum salts were applied to one axilla for several months and an inert vehicle was applied to the opposite control axilla. "With penicillin and streptomycin the staphylococci rapidly became resistant and deodorization is lost. Susceptible strains return to the axilla after treatment. The aluminum salt depresses the total count but does not alter the proportions of the resistant organisms. The use of neomycin alone or in combination with aluminum salts markedly suppresses the gram positive organisms and allows an overgrowth of gram negatives. The gram negatives which become dominant are those originally resistant to the antibiotic. Despite the change from a dominantly gram positive to a dominantly gram negative flora, deodorization is maintained as long as the antibiotic is used. With neomycin bacterial resistance, sensitization, superinfection and colonization by fungi did

Table 8

"SUCCESSIVE BACTERIAL COUNTS OF THE SAME AXILLA (MILLIONS/cm²)^a

Subject	<u>0</u>	<u>2 Weeks</u>	<u>4 Weeks</u>	<u>8 Weeks</u>
1	0.68	0.44	0.65	0.81
2	0.78	0.59	1.20	0.83
3	0.50	0.41	0.69	0.41
4	0.66	0.29	1.11	0.58
5	0.52	0.58	0.96	0.66
6	1.48	1.02	1.06	0.83
7	0.53	1.20	1.44	2.01
8	5.93	6.31	4.72	5.72
9	4.78	5.78	4.26	4.22
10	4.33	3.04	4.40	3.39
11	3.20	2.91	2.86	2.34
12	3.33	2.17	3.57	3.13
13	3.28	2.24	3.93	3.19
14	0.58	0.83	1.19	0.84
15	4.13	2.68	3.80	2.43
16	0.36	0.46	0.35	0.30
17	1.05	0.76	1.02	1.25
18	0.92	0.75	1.23	0.86
19	1.12	2.07	1.52	1.15
20	5.84	5.09	3.88	3.47
21	3.44	1.87	2.54	2.07
22	0.63	1.69	1.14	1.35
23	3.68	3.79	3.34	2.80
24	3.07	3.30	3.25	3.72
25	4.29	4.98	3.43	4.10
Avg.	2.36	2.21	2.30	2.10 "

a Shehadeh et al⁽²⁵⁾

Table 9

OCCURRENCE OF VARIOUS MICRO ORGANISMS ON AXILLA^a

Microflora	Subjects	1	2	3	4	5	6	7 ^b	8 ^b
Corynebacteria		x	x	x	x	-	x	x	x
Staph:									
phage + staph			x					x	
MSA + coag +		x	x					x	
MSA + coag -		x	x	x				x	x
MSA growth - no acid		x	x		x	x	x	x	x
Sarcina			x	x					
Micrococcus		x	x	x	x	x	x	x	x
Aerobacter A		x		x					
E. Coli					x				
Unident gram neg. rod					x				
Pro-actinomyces sp.					x	x		x	
Trichosporum			x						
a Effect of Diet & Atmosphere on Intestinal & Skin Flora (23)									
b control subject									

Staph = Staphylococci

MSA = Mannitol salt agar

Table 10

OCCURRENCES OF VARIOUS MICRO-ORGANISMS ON AXILLA^a

Subject Number	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
Micro-flora																	
Aerobacter		x	x	x													
PPLO													x				
Streptococcus	x																
Corynebacteria	x	x	x	x		x	x			x	x	x	x	x	x	x	
Micrococcus	x		x	x													
Bacillaceae	x			x		x	x		x	x							
Proactinomyces	x		x	x	x	x	x	x	x			x					
Neisseria		x	x	x	x										x		
Staphylococcus	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
Sarcina	x	x															
Obligate Anaerobes	x																
Fac. Anaerobes		x	x														
Mimae		x															
Yeast							x										
Gaffkya																x	
Helminthosporium sp.									x								
Mycelia sterila											x						
Nitrate neg. rod.									x								
Haemophilus								x									

^aBiomedical Criteria (AF33(615)-1814). (22)

Table 11

AXILLA - (BACTERIAL COUNTS)^a

Cult. Period

Subject no.	1	2	3	4	5	6	7	8	9	10
1	116,000	21,000	TNTC	TNTC	1,019,000	700	1,030,000	2,700	2,500	TNTC
2	2,600	TNTC	TNTC	10,100	12,100	TNTC	200	300	1,800	102,800
3	2,000	TNTC	TNTC	20,500	100,500	13,500	202,900	100,500	12,800	52,400
4	7,000	TNTC	TNTC	2,100	5,000	10,000	7,500	5,000	10,100	7,500
5	700	800	1,000	1,500	115,000	3,500	8,000	75,000	50,000	250,000
6	100	TNTC	1,000	25,000	150,000	7,500	300,000	200,000	TNTC	TNTC
7	3,500	TNTC	TNTC	39,500	40,000	TNTC	760,000	TNTC	507,000	10,000
8	400	TNTC	1,000	62,500	230,000	TNTC	70,000	TNTC	TNTC	TNTC

Counts equivalent to 10^{-3} bacteria^a Effect of Diet & Atmosphere on Intestinal and Skin Flora⁽²³⁾

not occur even after three months of daily use. Neomycin would appear to be a safe and effective deodorant in the above concentration."⁽²⁷⁾

Ear Microflora

The external auditory canal, as distinguished from the general skin area, is credited with the following flora by Rosebury⁽³⁾: Coagulase-negative staphylococci, coagulase-positive staphylococci, Strep. mitis and undifferentiated alpha and gamma streptococci, D. pneumoniae, aerobic corynebacteria, undifferentiated "coliforms", E. coli, Klebsiella aerogenes, Proteus mirabilis, Pseudomonas aeruginosa, Alcaligenes faecalis, Candida albicans and other candidas.

In a consideration of the flora of the external auditory canal, Singer, et al: (1952)⁽²⁸⁾ studied the flora of 1,377 normal external auditory canals and the following bacterial groups were recovered.

Table 12

MICROFLORA OF THE EXTERNAL AUDITORY CANAL

	<u>No. of Cultures Occurring</u>	<u>Percentage</u>
"1. Normal Ears		
Diphtheroids	374	17
Sporeformers	18	.8
Non-Hemolytic <u>Staph citreus</u>	26	1.2
Beta-Hemolytic <u>Staph citreus</u>	14	.6
Non-Hemolytic <u>Staph aureus</u>	33	1.5
Beta-Hemolytic <u>Staph aureus</u>	24	1.1
Non-Hemolytic <u>Staph albus</u>	1,065	48.1
Beta-Hemolytic <u>Staph albus</u>	1,420	64.5
Gamma streptococcus	515	23.4
Beta strep	2	.1
Alpha strep	4	.2
Paracolon group	2	.1
Alcaligenes group	24	1.1
<u>Coli-aerogenous sp</u>	90	4.0
Proteus	5	.2
Pseudomonas	29	1.3 "

In addition, these authors isolated Pityrosporum ovale in large numbers from the soft wax of the ear.

In a study by Hardy, et al: (1954)⁽²⁹⁾ on the etiological agents of otitis, pseudomonas, other gram-negative rods, and streptococcus were isolated. These organisms are present in the minority in the normal ear and the authors did not feel that otitis is the result of an autoinfection by the normal flora.

In the more detailed study by Slavin, et al: (1946)⁽³⁰⁾ of 100 cases of external otitis the following organisms were listed as causing external otitis:

Table 13

CAUSATIVE MICROORGANISMS OF EXTERNAL OTITIS

"Bacteria Present	Numbers
<u>Actinomyces israeli</u>	4
<u>Aspergillus niger</u>	3
<u>Aspergillus flavus</u>	4
<u>Aspergillus terreus</u>	4
<u>Pseudomonas species</u>	45
<u>Staph albus</u>	27
Unidentified diphtheroid	14
<u>Streptococcus viridans</u>	9
<u>Chromobacter species</u>	9
<u>Sarcina lutea</u>	2
Hemolytic streptococcus	2
<u>Staph aureus</u>	1 "

Pseudomonas species were not isolated from the normal ear canals of the controls.

In an effort to determine the mycological flora of the healthy external auditory canal, 120 subjects between the ages of 17 and 33 were examined by Lea, et al: (1958)⁽³¹⁾.

The following organisms were isolated:

Table 14

MICROFLORA OF EXTERNAL AUDITORY CANAL

'Types of Organisms Isolated	No. of Cultures	Frequency
<u>Homodendrum species</u>	6	20%
<u>Alternaria species</u>	3	10%
<u>Aspergillus species</u>	3	10%
<u>Candida albicans</u>	3	10%
<u>Candida species</u>	3	10%
<u>Saccharomyces</u>	3	10%
<u>Epicoccum species</u>	2	6.6%
<u>Ustilago zeae</u>	2	6.6%
<u>Cephalosporium species</u>	1	3.3%
<u>Penicillium species</u>	1	3.3%
<u>Pullularia pullulans</u>	1	3.3%
<u>Rhizopus species</u>	1	3.3%
<u>Scopulariopsis species</u>	1	3.3% "

In a recent study by Linthicum (1964)⁽³²⁾, 200 external auditory canals yielded positive cultures in 90% of the cases. The following bacteria were recovered:

Table 15

MICROFLORA OF EXTERNAL AUDITORY CANAL

'Types of Organisms Present	Percentage
Hemolytic <u>Staph aureus</u> Coagulase Negative	43%
Non-hemolytic <u>Staph aureus</u> coagulase negative	23%
Hemolytic <u>Staph aureus</u> coagulase positive	12%
Non-hemolytic <u>Staph aureus</u> coagulase positive	7%
Diphtheroids	6%

Table 15 (cont.)

MICROFLORA OF EXTERNAL AUDITORY CANAL

'Types of Organisms Present	Percentage
<u>B-subtlis</u>	2%
Staphylococcus	2%
Proteus	2%
Aerobacter	2%
Streptococcus	1% "

The data in Table 16 shows the flora isolated from the normal ear of the subjects in the Biomedical Criteria Study to be corynebacteria, Bacillaceae sp, pro-actinomyces, staphylococcus, and in certain subjects - micrococcus, lactobacillus, neisseria, mimae, sarcina, candida, and moraxella. The gram negative rods were conspicuous by their absence which is not in general agreement with the literature.

Eye Microflora

Two studies by Winkler, et al.^(33, 34) conclude that the normal flora of the eye is Staphylococcus albus, corynebacteria, Staphylococcus aureus, and occasionally gram negative rods, found in 8% of the subjects.

The results of the Republic Aviation Corporation study⁽²²⁾ on the normal flora of the eye show staphylococcus, occasionally E. coli, aerobacter, corynebacteria, micrococci, proactinomyces, neisseria, moraxella and in one instance each, an obligate anaerobe, and a facultative anaerobe to be present. (Table 17)

As summarized by Rosebury⁽³⁾ the microflora indigenous to the conjunctiva consists of: Coagulase-negative staphylococci, coagulase-positive staphylococci, Str. mitis, Str. pyogenes, D. pneumoniae, N. catarrhalis, aerobic corynebacteria, undifferentiated "coliforms" Klebsiella aerogenes, Proteus mirabilis, Alcaligenes faecalis, Moraxella lacunata, Mima polymorpha, M. vaginalis, Haemophilus influenzae and H. aegyptius.

Table 16
OCCURRENCE OF VARIOUS MICRO-ORGANISMS IN EAR^a

[illegible]

Table 17
OCCURRENCE OF VARIOUS MICROORGANISMS IN EYE^a

Subject Number	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
<u>Micro-flora</u>																	
<u>E. coli</u>		x													x		
<u>Aerobacter</u>		x															
<u>Streptococci</u>				x													
<u>Corynebacteria</u>	x	x		x													
<u>Micrococci</u>		x		x													
<u>Proactinomyces</u>						x											
<u>Neisseria</u>			x														
<u>Staphylococcus</u>	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
<u>Moraxella</u>		x			x			x									
<u>Fac. anaerobes</u>				x													
<u>Ob. anaerobes</u>	x																

^aBio medical Criteria (AF33(615)-1814). (22)

The bacteriology (as reflected by the normal flora) of the eye is of extreme importance to surgeons and most of the studies of the normal flora of the eye have been made for this reason. An exhaustive study of 1,604 patients who were pre-operative cataract patients was performed by Cason, et al: (1954)⁽³⁵⁾. The following organisms were recovered by Cason and Table 18 also includes the results of Khorazo and Thompson (1935)*.

The coagulase test performed on certain of the cultures showed that the S. albus was always negative, but that both hemolytic and non-hemolytic S. aureus were occasionally coagulase-positive. The authors felt that the skin was the most common source of the organisms. It is interesting to note that the percentage of gram-negative rods reported was greater than that found by other authors.

As shown by Winkler, et al: (1954)⁽³⁶⁾ in an attempt to relate post-operative infection to pre-operative flora of 1,653 cataract patients panophthalmitis developed post-operatively in 11 patients. In 10 of these cases, the causative organism was a gram-negative rod of the enteric group. 'The role of gram negative bacilli as 'opportunists' in causing infection was suspected after the first case of panophthalmitis. Subsequent infections confirmed the potential pathogenicity of members of the enteric group of bacilli. "

In an effort to establish the bacteriological causes of infection following the use of contact lenses, Bettman (1963)⁽³⁷⁾ cultured the fornices of the eye of 69 control subjects: of these, 36 were sterile, 31 carried Staph. aureus, 2 carried Staph. albus, 4 carried alpha or gamma hemolytic strep, 2 carried diphtheroids, and 1 carried B. subtilis.

An interesting study was performed by Das, et al: (1955)⁽³⁸⁾ who studied the bacteriology of the conjunctival discharge of 50 persons. In addition, the discharge from meibomian glands in 25 normal persons as well as washings from the lachrymal sac in 25 subjects were studied and the bacterial flora of the external auditory meatus was determined in 25 normal subjects and compared with the findings from 100 cases of corneal ulceration (Table 19).

* Khorazo, D.; and Thompson, R.: Am. J. Ophthalmol., vol. 18, 1935, pp. 1114.

Table 18

MICROFLORA OF EYE

" Organism	Conjunctiva		Lids		Results of K&T *
	No.	Percent	No.	Percent	Percent
<u>Staph albus</u>	1097	68	1531	95	41
<u>Staph aureus</u>	105	7	199	12	23
<u>Micrococcus citreus</u>	7	1	15	1	--
Diphtheroids	531	33	612	40	36
Sarcina	19	1	58	3	1
<u>Strep. pyogenes</u>	4	1	2	1	1.2
<u>Strep. viridans</u> (sp.)	7	1	4	1	3.4
Indifferent strep.	2	1	3	1	--
Pneumococcus	8	1	7	1	2.6
<u>Neisseria catarrhalis</u>	3	1	10	1	--
<u>Neisseria sicca</u>	3	1	4	1	--
<u>B. subtilis</u>	5	1	26	2	(9)
<u>A. aerogenes</u>	21	1	25	2	(1)
<u>P. vulgaris</u>	19	1	24	1	(6)
<u>Pseudomonas aeruginosa</u>	8	1	11	1	(4)
<u>E. coli</u>	3	1	3	1	(5)
<u>A. faecalis</u>	1	1	3	1	(3)
<u>K. pneumoniae</u>	0	--	3	1	--
Unidentified Gram Negative Rods	23	1	38	2	--
<u>Monilia (Candida)</u>	2	1	3	1	(5)
Cryptococcus	1	1	0	1	(5)
No Growth	374	23	45	3	(17)

() = Actual Number, Not Percent "

* Khorazo, D.; and Thompson, R.: Am. J. Ophthalmol., vol. 18, 1935, pp. 1114.

Table 19

RESULTS OF CULTURES BY DAS

"	No. Occurring	
Normal Conjunctiva:	pneumococcus	6
	<u>Strep. viridans</u>	3
	<u>Staph. pyogenes</u>	2
	<u>C. xerosis</u>	29
	Non-pathogenic staph	19
	Negative	16
Meibomian Glands:	Pneumococcus	2
	<u>Strep. viridans</u>	4
	<u>Staph. pyogenes</u>	2
	<u>C. xerosis</u>	10
	Non-pathogenic staph	8
	Micrococci	1
	Non-hemolytic strep	1
	Negative	9
Lachrymal Sac:	<u>Strep. viridans</u>	1
	<u>C. xerosis</u>	8
	Non-pathogenic staph	12
	Micrococci	1
	<u>N. catarrhalis</u>	1
	Negative	8
External Auditory Meatus	<u>C. xerosis</u>	10
	Non-pathogenic staph	17
	<u>Micrococcus tetragenus</u>	3
	Negative	3

Table 19 (cont.)

RESULTS OF CULTURES BY DAS

	No. Occurring
Corneal Ulcer:	
Pneumococcus	8
<u>Strep. viridans</u>	8
<u>Staph. pyogenes</u>	31
<u>C xerosis</u>	35
Non-pathogenic staph	22
<u>Strep. haemolyticus</u>	2
<u>B. pyocyaneus</u>	14
<u>M. tetragenus</u>	3
<u>N. catarrhalis</u>	1
Non-haemolytic strep	1
* Negative	19

* Note: 5 of the 19 showed either gram positive cocci or gram positive bacilli on smear. "

Finger and Toenail Microflora

The normal bacteriological flora of the finger or toenail has never been completely defined since most of the studies have dealt with the organisms present in paronychia or similar condition and with the fungi of the toewebs rather than of the toenail. The only references reviewed revealed that histopathology results from penetration of the epidermis in the vicinity of the nail and the nail itself seems to be sterile (Stone, et al: (1962 and 1965)^(39, 40). In a further investigation of the role of Pseudomonas aeruginosa in nail disease, the following organisms were recovered in culture with pseudomonas by Stone, et al: (1963)⁽⁴¹⁾: "Candida albicans, Geotricum species, Pseudomonas aeruginosa, Proteus mirabilis, Alpha hemolytic streptococcus, streptococcus (enterococci group), gamma hemolytic streptococci, Escherichia intermedium, Micrococcus species, Sarcina species, Aerobacter aerogenes, Paracolobacterium aerogenes, as well as unidentified gram negative rods and diphtheroids. "

The predominant interdigital flora of the toeweb as shown in Table 20 seems to be composed of staphylococcus, corynebacteria, proactinomyces, and occasionally micrococci, bacillaceae, and various members of the fungal family.

Scalp Microflora

In a thorough study of the scalps of 100 individuals by MacKee, et al: (1938)⁽⁴²⁾, an interesting separation of the numbers of differing kinds of microorganisms was possible on the basis of whether the scalps were: (1) "normal", (2) dry with a hair loss, (3) oily, or (4) showed seborrheic eczema. The results of this study are summarized in Table 21.

It is interesting to note the high percentages of anaerobic diphtheroids and scurf staphylococci in alopecia. This author's work was in agreement with the findings of Templeton (1926)⁽⁴³⁾.

Further work on Pityrosporum ovale was done by Spoor, et al: (1954)⁽⁴⁴⁾ who found this organism present in 60% of the subjects, but felt that proof was lacking for the indictment of Pityrosporum ovale as a causative agent of dandruff. Work was done on several hundred scalps both normal and seborrheic in the age bracket of 15-55 years. When the subjects were separated by age category the incidence of P. ovale was 70% up to the age of 45 years and 40% between the ages of 45-60.

The "scalps" cultured during the Air Force study⁽²²⁾ yielded a flora mainly composed of corynebacterium and staphylococci with sporadic occurrence of other micro-organisms as shown in Table 22.

Umbilicus Microflora

No papers on the microflora of the umbilicus were found in the literature, but the flora of the umbilicus as shown by Republic Aviation Corporation studies is recorded in Table 23 and consisted mainly of staphylococci with sporadic appearance of streptococci, corynebacteria, micrococci, bacillaceae, proactinomyces, and neisseria.

Table 20

OCCURRENCES OF VARIOUS MICRO-ORGANISMS ON TOES^a

Subject Number	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
<u>Micro-flora</u>																	
<u>E. coli</u>																x	
<u>Corynebacteria</u>	x			x					x	x	x	x	x			x	
<u>Micrococci</u>				x													
<u>Bacillaceae</u>						x											
<u>Proactinomyces</u>	x		x		x	x	x	x									
<u>Staphylococcus</u>	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
<u>Yeasts</u>			x														
<u>T. rubrum</u>					x												
<u>Penicillium sp.</u>											x		x				
<u>Pseudomonas</u>														x			
<u>T. mentagrophytes</u>															x		
^a Biomedical Criteria (AF33(615)-1814).																	

Table 21
" SCALP FLORA ^a

	<u>Number</u>	<u>Scalp</u>	<u>Roots</u>
1. Normal	20		
<u>Staph albus</u>		70	25
<u>Staph epidermis</u>		20	--
<u>Scurf staph</u>		50	30
<u>Staph aureus</u>		10	--
Diphtheroids		5	15
Unidentified		55	25
<u>Pityrosporum ovale</u>		70	--
2. Dryness with Hair Loss	33		
<u>Staph albus</u>		81	21
<u>Staph epidermis</u>		6	3
<u>Scurf staph</u>		90	39
<u>Staph aureus</u>		6	--
Diphtheroids		3	62
Unidentified		30	33
<u>Pityrosporum ovale</u>		97	--
3. Oiliness	10		
<u>Staph albus</u>		80	10
<u>Staph epidermis</u>		20	10
<u>Scurf staph</u>		70	50
<u>Staph aureus</u>		--	--
Diphtheroids		--	70
Unidentified		20	20
<u>Pityrosporum ovale</u>		100	--

a MacKee et al (1938)⁽⁴²⁾

Table 21 (cont.)

	<u>Number</u>	<u>Scalp</u>	<u>Roots</u>
4. Seborrheic Eczema	50		
<u>Staph albus</u>		50	12
<u>Staph epidermis</u>		12	--
<u>Scurf staph</u>		12	24
<u>Staph aureus</u>		12	24
Diphtheroids		12	62
Unidentified		62	50
<u>Pityrosporum ovale</u>		75	--

The fungi found irregularly were:

Aspergillus
 Macrosporium
 Alternaria
 Rhizopus
 Chaetomium
 Mucor
 Cryptococcus
 Torula
 Dematium
 Mycoderma "

a MacKee et al (1938)⁽⁴²⁾

Table 22
OCCURRENCE OF VARIOUS MICRO-ORGANISMS ON SCALP^a

[illegible]

Table 23

OCCURRENCE OF VARIOUS MICRO-ORGANISMS IN UMBILICUS^a

Subject Number	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
<u>Micro-flora</u>																	
<u>Streptococci</u>			x	x													
<u>Corynebacteria</u>			x				x						x		x		
<u>Micrococci</u>	x	x	x														
<u>Bacillaceae</u>							x	x			x						
<u>Proactinomyces</u>							x	x									
<u>Neisseria</u>	x		x														
<u>Staphylococcus</u>	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
<u>Fac. anaerobes</u>			x														
<u>Penicillium sp.</u>											x						
<u>Scopulariopsis</u>									x								
^a Biomedical Criteria (AF33(515)-1814). (22)																	

Borderline Between Normal and Pathogenic Microflora

Since the borderline between normal and potentially pathogenic skin flora is so close the various articles reviewed including those on fungi, viruses and staphylococci, will be treated in this section rather than in the section on normal flora.

Mycological Flora

The mycological flora of the skin is important both from a medical and endemological viewpoint.

In an effort to establish this "normal" mycological flora of the skin, many papers were reviewed and those considered most pertinent will be discussed. Connell, et al: (1953)⁽⁴⁵⁾ cultured 250 normal subjects between the ages of 17 and 30 (unbathed for 3 days) from the axilla, lumbar region, inframammary area, umbilicus, and between the fingers and toes. One thousand one hundred twenty-one (1,121) organisms were isolated. These included Cryptococcus aerius, Cryptococcus minor, Cryptococcus rotundatus, Lycomyces starkeyi, Candida mesenterica. The following organisms were isolated from the body and the air: Cryptococcus albidus, Cryptococcus diffluens, Cryptococcus laurentii, Cryptococcus var. flavescens, Cryptococcus luterhu, Candida lepolytic, and Candida zeylanoides. The largest number of recoveries was from the toe area closely followed by the fingers and roughly equal recoveries from the other body areas.

Benham, et al (1933)⁽⁴⁶⁾, in an attempt to define the etiological relationship of fungi recovered from the skin to the flora of the intestinal tract studied 100 "normal" individuals. He recovered yeast-like fungi from 72%; in 38, two or more species were recovered from the skin and nails and in 23, cryptococci were recovered from two differing skin areas. He could establish no relationship between the intestinal flora and that of the skin except in two instances of Candida. He discussed the paper by Greenbaum, et al: (1922)* who studied 150 "normal"

*Greenbaum, S.S.; and Klauder, N.V.: Yeast Infections of the Skin. Arch. Dermat. Syphilol., vol. 5, 1922, pp. 332-336.

patients who yielded 35 strains of yeast-like fungi. They concluded that yeasts were found normally, and under certain circumstances the yeasts became pathogenic and caused superficial infections. In addition Benham reviewed the paper of Jessner, et al: (1925)**, who had found fungi under the fingernails of 60% of the "normal" population in agreement with the findings of Stachlin, et al: (1932)***. In direct opposition to these articles is the work of Falchi (1926)**** who found fungi under the nails of only 10% of the "normal" population. Another pertinent paper mentioned by this author was that of Ravaut, et al: (1929)***** who had observed 150 "normal" individuals and cultured yeast-like fungi from approximately 75%.

Increase in the absolute quantities of sebum on the surface of the scalp which occurs after puberty is a factor in the immunity of adults to certain types of scalp ringworm. It seems probable that the fatty material is presented to the skin population in the form of triglycerides, and that members of the community which occupy the fat-splitting ecological niche, hydrolyze the triglyceride, thus producing free fatty acids with anti-microbial powers.

One of the principal investigators who dealt with the position of dermal fungi was diMenna who, in one of her many studies (1954)⁽⁴⁷⁾, found the non-lipophilic yeast flora of the skin was like that of the air, both in species and proportion and found that the four dominant species were Debaryomyces sp., Cryptococcus sp., Rhodotorula sp., Cladosporium sp.

In a study by Skinner, C.E.; Connell, G.H.; and Hurd, R.M.: (1952) (quoted from di Menna) yeasts were isolated from 50% of 275 persons repeatedly, and the

** Jessner, M.; and Kleiner, S.: Arch. F. Dermat-u. Syph., vol. 149, 1925, pp. 363.

*** Stachlin, A.; Mu, J.W.; and van Schouren, M.: Arch. F. Dermat-u. Syph., vol. 165, 1932, pp. 294.

**** Falchi, G.: Arch. F. Dermatol-u. Syph., vol. 152, 1926, pp. 427.

***** Ravaut, P.; Rabeau, H.; Longhin; and Slomovici, L.: Bull. Soc. franc de Dermat et Syph., vol. 36, 1929, pp. 607.

authors felt that the cultures originated in the environment. Of the positive cultures 10% were Rhodotorula sp., 85% were cryptococcus, and 5% miscellaneous.

In a study of Pityrosporum ovale, Spoor, H.J., et al (1954)⁽⁴⁴⁾ found this organism present in 60% of the persons, and felt that was not related to seborrheic infection, but that the age susceptibility may play a part. In a study of 196 males, up to age of 45 about 70% of the males showed positive cultures of P. ovale, between ages 45-60 less than 40%, above 60 years of age 70%.

Ravits (1948)⁽⁴⁸⁾ studied 100 patients with various dermatoses and 100 'normal' controls. Seventy-five percent of the 'normals' carried cryptococcus while only 54% of the patients with the dermatoses exhibited positive cultures. This is in contrast to Felsenfeld (1944)* who found cryptococcus in 30% of his 'normal' controls. In Ravits' study⁽⁴⁸⁾ the toes and fingers were about equally infested while the umbilicus and axilla showed half as much and the inframammary region had none.

In a recent study by Bohme (1965)⁽⁴⁹⁾, 11.6% of the hair and nails of his subjects were infected with fungi; i. e., dermatophytes. Only one-third of these were identified and they fell into the following groups: Trichosporon cutaneum, Debaryomyces kloeckeri, Candida parapsilosis, Candida albicans, rhodotorula, torulopsis, and Candida guilliermondii.

As part of the study by Blank (1964)⁽⁵⁰⁾, 100 subjects were sent from Virginia to Panama for a period of six weeks. After their stay in Panama 60% of the men had pathogenic fungi somewhere on their skin, 50% had erythrasma of the toe webs, and 12% had significant pseudomonas infection of the skin. It is felt that mosquitoes, ants, and flies helped in the spread of these troublesome cutaneous bacterial infections.

Friedman (1960)⁽⁵¹⁾, in a study of a large number of children, found that approximately 56% had positive cultures of dermatophytes, but only 22% were actually infected as determined by finding endothrix or ectothrix hairs which could be confirmed by fluorescence with Wood's light.

* Felsenfeld, O.: Amer. J. Med. Sci., vol. 207, Jan. 1944, pp. 60.

In an examination of 839 subjects, Carion (1963)⁽⁵²⁾ found the following distribution of ringworm:

Table 24
DISTRIBUTION OF RINGWORM

" <u>Tinea pedis</u>	327 cases	39% of total
<u>Tinea unguium</u>	202	24.1%
<u>Tinea corporis</u>	172	20.5%
<u>Tinea capitis</u>	97	11.6%
<u>Candidiasis</u>	18	2.1%
<u>Tinea nigra</u>	11	1.3%
<u>Tinea nodosa</u>	7	0.8%
<u>Tinea barbae</u>	5	0.6% "

Only five cases of skin candidiasis were found between 1939 and 1949.

The indigenous character of Candida has often been in question. An interesting case of an infant born with moniliasis without prior known rupture of the membrane is reported by Jahn and Cherry (1964)⁽⁵³⁾.

In a search to establish the prevalence of Candida albicans, Marwin (1949)⁽⁵⁴⁾ cultured 200 normal subjects, average age 25 years and 109 "pathological" (average age of 45). He found only 1.5% of the "normals" carried Candida albicans as compared to 6.4% of the "pathologicals" who carried it. The majority were isolated from the skin of the toes, axilla, umbilicus.

One of the largest groups of men to be examined for the determination of the presence of skin disease or dermatomycosis were in a series studied by Cullen (1963)⁽⁵⁵⁾ (Table 25).

The endemic or epidemic character of Tinea capitis is an interesting problem and the study performed by Kallos (1962)⁽⁵⁶⁾ summarizes the importance of Tinea capitis among the dermatophytes, since an extremely large portion of the population

Table 25

PRESENCE OF SKIN DISEASE

" Pyoderma Group	123	0.46%
<u>Herpes Simplex</u>	19	0.07%
Leprosy of skin	1	0.0004%
Syphilis of Skin	2	0.007%
<u>Verruca vulgaris</u>	180	0.67%
Zoster	4	0.01%
The dermatomycosis:		
Total: 1,580	5.92%	
<u>Tinea versicolor</u>	1,171	4.39%
<u>Tinea cruris</u>	286	1.07%
<u>Tinea pedis</u>	40	0.15%
<u>Tinea circinata</u>	14	0.05%
Onychomycosis	8	0.03% "

of varying countries is affected and until recently man seemed unable to fight the disease with any appreciable success. The geographic distribution is admirably summarized in the following chart. (Table 26).

In a further geographical survey, Chaglassian, et al: (1962)⁽⁵⁷⁾ discusses the epidemiology of the cutaneous diseases in the Middle East. He studied 2,652 patients. Only 7% of these showed skin diseases of bacterial origin while 12% of the skin diseases could be traced to mycotic causal agents. The cultural distribution of the dermatophytes is summarized in the following chart (Table 27).

Several papers considering the factors affecting infection with fungi were reviewed.

In order to determine the indigenous character or the susceptibility to infection with Tinea versicolor, Burke's (1961)⁽⁵⁸⁾ study determined the following causal factors: (1) genetic, (2) chronic illness, (3) malnutrition, (4) lack of

Table 26

" RELATIVE INCIDENCE OF FUNGI CAUSING TINEA CAPITIS EXCLUSIVE
OF TRYCHOPHYTON SCHOENLEINI^a

Country	Microsporum			Trychophyton		
	Canis	Audouini	Violaceum	Tonsurans*	Mentagr.	Ferrugineum
France	+++	++++	+	++		
Spain	+		++++	++		
Portugal	+		++++	++		
Italy	+	++	++++	++		
Yugoslavia		+	++++	+		++
Greece			++++			
Turkey	++++	+	+	+		
Israel			++++	++		
Iran			++++			
Egypt			++++	+		
Libya			++	+++		
Tunisia		+	++++	++		
Algeria		+	++++	++		
Morocco		+	++++	++		
Cameroun		+	++++	++		
Haute Volta		++	+++	++++		
Tchad		+	++	++++		
Guinea		+	++	++++		
Ivory Coast		++++		+++		
Nigeria		++++				
Angola			+	++		++++
Congo			+	++		++++
South Africa	++++		+			
India		+	++++	+	++	++
Malaya	++		++++	+		+++
U. S. S. R.	++		++++	+		+++
Japan			++	+		++++
Australia	++++	+	+	+		
New Zealand	+++	+	+	+		

^a Kallas (1962)(56)

Table 26 (continued)

RELATIVE INCIDENCE OF FUNGI CAUSING TINEA CAPITIS EXCLUSIVE
OF TRICHOPHYTON SCHOENLEINI^a

Country	Microsporum			Trychophyton		
	Canis	Audouini	Violaceum	Tonsurans*	Mentagr.	Ferrugineum
England	++++	+++	+	+		
Ireland	+++	+++				
Denmark	+++	+				
Finland	+		++++	++		
Germany	+	++++	+	++		
Holland	++++	+				
Belgium	+++	++				
Switzerland	++	+				
Hungary	++++	++	+++	++		
Poland		+	++++	+		
Checkoslov.	+		+	+	++++	+
Rumania			++++	+		
Bulgaria			++++			
Peru	++++		+	+		
Argentina	++++		+	+		
Chile	++++	+				
Uruguay	++++		+	+		
Brazil	++++		+++	++		
Venezuela	++++			++		
Mexico	+			++++		
El Salvador				++++		
Guatemala	+++			+		
Honduras	+++			+		
Nicaragua	+++			+		
Costa Rica	++++			+		
Cuba	++++			+++		
Jamaica		++++				
U. S. A.	+++	++++		+		
Porto Rico	+	+		++++		
Canada	++++	+++		+		

* Trichophyton tonsurans, Trichophyton soudanensi and Trichophyton Yaoundei were included under the same heading."

a Kallas (1962)(56) "

Table 27

" CULTURAL DISTRIBUTION OF DERMATOPHYTES ^a

	<u>C. albicans</u>	<u>T. rubrum</u>	<u>T. violaceum</u>	<u>T. mentag.</u>	<u>T. tonsurans</u>	<u>T. verrucos</u>	<u>T. schoenleinii</u>	<u>E. flocc</u>	<u>M. gypseum</u>	<u>M. canis</u>	TOTAL
Nails	31	7	-	-	-	-	-	-	-	-	38
Oro-ano-genital*	20	-	-	-	-	-	-	-	-	-	20
Hands & Interdigital**	11	6	2	1	2	-	-	1	-	-	23
Feet	12	9	1	19	-	-	-	4	-	-	45
Groin	20	17	2	5	-	-	-	35	-	-	79
Body	9	25	4	10	1	-	1	8	-	-	58
Scalp	-	4	21	2	3	1	3	-	8+	3++	45
TOTAL	103	68	30	37	6	1	4	48	8	3	308 "

* Includes angle of the mouth.

** From palmar lesions.

+ Repeated cultures from two patients.

++ Repeated cultures from one patient.

^a Chaglassian (1962)⁽⁵⁷⁾

vitamins, and (5) changes induced by abnormally high indigenous or administered plasma cortisone levels.

A study of 297 women by Buck and Hasendiver (1963)⁽⁵⁹⁾ to determine the relative sensitivity and specificity of skin and agglutination tests in relation to the presence or absence of Candidiasis and of the saprophytic growth of the fungus, resulted in the conclusion that there was a negative association between the size of the induration and the skin reaction and agglutination titers.

An effort was made to simulate infection by the inoculation of various dermatophytes on hair, and an interesting conclusion was drawn to the effect that appearance of the invasion by dermatophytes is different in simulated infection than that of actual disease. It was felt by Raubitschek (1963)⁽⁶⁰⁾ that the common dermatophytes such as Trichophyton-mentagraphytes, Trichophyton rubrum, Trichophyton tonsurans, Trichophyton violaceum, Trichophyton schoenleini, and Epidermophyton floccosum were present without disease in many subjects.

Viral Flora of Skin

The common viral inhabitants of the skin are numerous and the part that they play in the ecology of the microflora has never been clearly defined. Much further work is necessary to clarify the part they play in the economy of the skin.

Several members of the poxvirus group can become temporary inhabitants of the skin and one, Poxvirus mollusci lives only in the layers of the skin and possibly is a true member of the cutaneous biocenose.⁽⁶⁾ In addition to causing tumor like growths on the skin it can infect the conjunctiva. It is possible that members of this group have an inhibitory effect on the growth of pathogenic bacteria but no detailed information exists on this possibility. Marples' view is that, since these poxviruses are present without apparent infection in large numbers, they may be members of the normal flora.

Herpesvirus Hominis is a virus which may be considered to fall within a discussion of the normal biota of the skin. In more than 90% of the population an attack of herpesvirus has no symptoms and is sub-clinical in nature. Its identification is made by demonstrating a specific antibody. However, after an invasion,

whether asymptomatic or symptomatic, the virus remains quiescent for the duration of the host life. Whenever the resistance of the host becomes sufficiently lowered the herpesvirus may easily cause symptoms. Marples⁽⁶⁾ states that "Herpesvirus hominis is an extremely successful and well adapted parasite of man. It is able to invade the superficial tissues of the majority of individuals and can so enter into the life of the host cells that it survives and divides with them unrecognized, except during a few fleeting incidents when multiplication and dissemination can occur. "

Bacterial invasion of a herpes lesion has not been recorded. In a recent publication, Schneierson and Shore,⁽⁶¹⁾ demonstrated that antibacterial activity was possessed by the herpesvirus in vitro and this activity may be responsible for the lack of bacterial invasion of herpes lesion.

Another common skin lesion produced by virus is a wart. It is believed that these viruses are members of the Papova group. Recent studies revealed information on the etiology of warts and it is felt that infective particles are often present without frank wart formation, as they can inhabit the epidermis without substrate change.

Plantar warts, as studied by Grigg & Wilhelm⁽⁶²⁾ revealed the high incidence of 4.47% in the normal school population of 2,389 children. The authors felt that approximately 23% of the families with school aged children included wart viruses among their skin flora.

An excellent summary of virus infections of the skin by Church (1964)⁽⁶³⁾ serves to focus attention on the fact that "Bacterial and fungus diseases of the skin are no longer the problem they once were. Of virus diseases we know a great deal concerning the organisms and the serological reactions which they provoke but when it comes to treatment we are no further forward than Kebra (1866) "Experience then teaches that an expectant treatment is the best, so long as an herpetic eruption is present. "

A survey of East Anglian schools revealed an incidence of plantar warts of approximately 6.5% and other warts 10%. The plantar warts were twice as

numerous in girls as in boys and it was felt that was not a sex-linked characteristic but rather due to the fact that girls were bare-footed during gymnastics.

"The herpes simplex virus can produce a secondary infection on skin damaged by eczema." (63)

"The concept of a primary infection followed by a dormant virus which can be provoked into activity by a variety of stimuli has been illustrated by the example of herpes simplex. The same sequence of events is thought to occur in herpes zoster, the primary infection being chickenpox." (63)

Staphylococci

Since one of the predominating members of the skin flora are the various staphylococci strains, it is essential to consider the possible conditions underlying the transition from normal to pathologic flora. Many excellent papers deal with varying aspects of this problem and representative areas will be reviewed.

In an attempt to define the parameters in this transition Bowers, R. E.; (1964)⁽⁶⁴⁾, in a study of the pyogenic infections of the skin, felt that although the skin resistance to bacterial invasion and damage is great, its powers of surface disinfection are very limited. Most of the areas which are considered to be "carrier" sites are moist, warm places; i. e., anterior nares, axillae, and perineum. Pathogenic bacteria growing on these areas do not necessarily cause manifest disease in the host or his contacts, but when they do, they appear to achieve this state by being spread in such large numbers that the natural defenses are overwhelmed. There seems to be some correlation between carrier sites and areas affected by the disease; i. e., recurrent boils of the thighs and groin area would signify perineal carriage; a lesion on the face or neck - nasal carriage.

The author⁽⁶⁴⁾ felt that the predisposing factors to staphylococcal infection are the following:

1. Eczema
2. Nasal folliculitis, fissures behind the ears
3. Poor personal hygiene
4. Parasitic infection

In an effort to establish the self-sterilizing power of the skin, Ricketts, et al: ⁽⁶⁵⁾ performed a series of in vitro experiments demonstrating the bactericidal powers of fatty acids on cultures of pathogenic streptococci and staphylococci.

One of the parameters necessary for pathogenicity of an organism is its ability to become established and sustained by the host. For example, as mentioned by Panos, (1963) ⁽⁶⁶⁾, staphylococcus has the following prominent exotoxins: enterotoxin, leucocidin, hemolysins, coagulase, fibrinolysin, hyaluronidase, deoxyribonuclease are also present in strains of staphylococcus, but their ability to cause disease is in proportion to the ease with which an infectious process can become established. Usually, this is the result of physical injury or an alteration in the host resistance or an increased susceptibility to the pathogen.

Juhlin (1965) ⁽⁶⁷⁾ feels there is a connection between hygienic measures used and the incidence of infection in thousands of hospital patients. An extensive study demonstrated the necessity of isolating any patient with a staphylococcal infection and of the hospital personnel wearing protective coats and gloves and using a "bac" wash. They felt that pHiso-Hex ^(R) was one of the best germicides.

In a study in Turkey, Cetin (1962) ⁽⁶⁸⁾ demonstrated that many individuals are carriers of potentially pathogenic bacteria, particularly on the skin, which might cause auto-infection when a favorable background is available. In particular, those strains that are antibiotic-resistant are responsible for infection in individuals whose resistance is low. He was able to phage type 225 strains of Staphylococcus aureus recovered from skin infection.

Popchrestov, P., et al: (1965) ⁽⁶⁹⁾ performed an interesting experiment by tagging staphylococci with P32 in order to determine the spread of the organisms. It was felt that the normal skin flora possessed an antagonistic action which prohibited the growth of the organism since the spread of staphylococcus was so minute on the borders of colonies, that a Geiger counter could not follow the P32 marked staphylococci. In addition the cultures possessed a weakened biological characteristic after growth on the skin.

In another approach, Wallace, H.J. (1964)⁽⁷⁰⁾ felt that many cases of chronic staphylococcus infection suggest "seborrhoeic background" possibly an inherited tendency of the skin to break down in characteristic areas which are well supplied with sebaceous and sweat glands. Such breakdown may be precipitated inter alia by systemic infections, excessive sweating, or a secondary infection. It is possible that a carrier state may exist in the peri-anal area as well as the nares. Less frequently, carrier states have been found in the axilla, fingernails, ears and sometimes even in the margin of the eyelids.

The possibility of susceptibility to staphylococci infection being a sex linked characteristic has been explored in a recent study by Thompson, et al: (1963)⁽⁷¹⁾. This exhaustive study dealt with 2,147 newborn infants of which 1,938 were followed for a substantial period. The frequency of colonization of males by Staphylococcus aureus ranged 6.4% higher than in females and there were 2.7 sites per diseased male. The localization of the lesions in the male were in the anterior diaper area, the groin, the superpubic area and the lower abdominal area, while in the females the eye was the most frequently infected area, followed by the face.

Among the few studies directed at establishing the relationship of the size of inoculum to the lesion is the fine work of Elek⁽⁷²⁾.

In a study of the "Problems of the Initiation of Dermal Staphylococcal Lesions", Elek⁽⁷²⁾ attempted to elucidate the nature of the interaction between the microbe and the man, and used the hypothesis that in vitro and in vivo effects on animal cells could possibly explain the production of lesions in man. In vivo, he found it was necessary to use 5 million cocci to produce a pustule. In rabbits, the dosage was ten times greater. The chemical basis of the virulence of staphylococci is different in man and rabbits and it is a fallacy to try to project in vitro results in rabbits to in vivo results in humans. The author postulated that an intermediate mechanism allowing a small inoculum to multiply for a few hours unhindered was necessary to produce a dermal lesion and for this reason felt that the answer was in the host rather than in the parasite.

Another interesting observation of Elek (1965)⁽⁷²⁾ was the fact that it required 7.5×10^{-6} Staphylococcus pyogenes microorganisms when introduced by interdermal injection to consistently produce pus formation, but a single

suture contaminated with roughly 100 microorganisms consistently produced a pustular lesion.

The potential pathogenicity of a staphylococcal strain is an important factor in any definition of infection. Elston's (1964)⁽⁷³⁾ study was a determination of the physiological characteristics in relationship to the pathogenicity of the culture. The DNASE activity paralleled the coagulase reaction in 98.8% of the cultures while the manitol salt agar fermentation paralleled the coagulase reaction in only 85.9%. The mannitol broth fermentation paralleled the coagulase reaction in 97.17 of the cultures if they were incubated from 2 to 7 days.

Many authors believe that Staphylococcus aureus is a more prevalent member of the skin biota than is commonly supposed. In a study by Kudsini, et al: (1963)⁽⁷⁴⁾ 388 subjects showed a 57% rate of Staphylococcus aureus skin infection, and 25.6% had some active infection such as boils, impetigo, mastitis, pimples, etc. The author cultured the washing of these subjects and found that after home laundry at 55-64°C a recovery of 80,000 to 84,000 staphylococcus per ml was achieved and this could account for the intrafamily incidence of Staphylococcus aureus.

In the differentiation of strains occurring in the body, Rosendal (1963)⁽⁷⁵⁾ has shown that the skin strain predominated in all age groups for all cultural sites.

Table 28

STAPH STRAIN RECOVERED

" Body Area	No. of Cultures	Percentages	Phage Type 83A
Hands	472	6.8	2
Eczema & Skin Diseases	12	0.2	1
Eye	119	1.7	0.8%
Ear	240	3.4	6 "(75)

In an effort to characterize the skin strain of staphylococcus, Jones, et al:⁽⁷⁶⁾ based their differentiation on a study of Staphylococcus epidermis on the following points: (1) the ability to grow anaerobically in a glucose media, (2) an inability to

produce coagulase, and (3) an inability to ferment mannitol anaerobically. These authors found that 93% of the Staphylococcus epidermis isolated required uracil for anaerobic growth.

A logical corrolary to the definition of the normal flora is the use of this flora to prevent or circumvent infection. Many papers on implantation of staphylococcus have been written by Shinefield and his associates. In a recent review an editorial of JAMA⁽⁷⁷⁾ states that Shinefield and his associates (1964) demonstrated the phenomenon of microbial interference by implantation of one strain of Staphylococcus aureus at a particular site (nasal or umbilical) and showed that this produced an immunity or pre-immunization against other strains of Staphylococcus aureus. This technique is of particular importance in the prevention or termination of staphylococcal epidemics in the nursery for the newborn.

In a study of epidemic staphylococci Rycheck (1963)⁽⁷⁸⁾ found that staphylococcus with a group 2 pattern produced severe exfoliative dermitis. He considered Ritter's disease to be a staphylococcal skin disease with a group 2 phage pattern. The authors reported a severe nursery infection and classified the appearance of the staphylococci that appeared.

In a study of 1,000 patients by Mirolynbov, V.I.: (1960)⁽⁷⁹⁾ it was found that the most common sites of pyodermic foci were the exposed skin areas, especially the face, because of the ease with which cocci from oral and nasal cavities infect the face, as well as the disregard for rules of personal hygiene while shaving and using cosmetics.

Actinomyces - Pro-Actinomyces Group

The part played by members of the actinomyces and pro-actinomyces or Nocardia groups in the normal flora is ill-defined. In Krassilnikov's, N.A.: (1949)⁽⁸⁰⁾ book, sufficient recovery of various pro-actinomyces i.e. P. gedanensis, P. pinoyi, P. pangenensis as well as P. dicussatus from the skin of man seems to give some basis for their inclusion in the normal flora, either as permanent or transient members.

Rosebury, T.: (1958)⁽⁸¹⁾ feels that the obligately indigenous character of actinomycetes has become accepted, at least as far as mucous membranes are concerned, but does not list them among the normal skin flora.

During the Republic Aviation studies⁽²²⁾ ⁽²³⁾, members of the pro-actinomyces group were recovered with sufficient frequency to feel that their indigenous character should be elucidated.

Pathogenic vs Normal Flora

Sometimes microflora considered to be normal may cause frank infections, while in other instances pathogens appear to become part of the normal flora. Several papers tell of specific instances of such occurrences.

In a series of 1,653 cataract patients, an attempt was made by Winkler (1959)⁽⁸²⁾ to relate post-operative infection to the pre-operative flora or exogenous source. Panophthalmitis occurred post-operatively in 11 patients. In 10 of these cases, the causative organism was a gram negative rod of the enteric group. 'The role of gram negative bacilli as 'opportunists' in causing infection was suspected after the first case of panophthalmitis. Subsequent infections confirmed the potential pathogenicity of members of the enteric group of bacilli. "

Miles A. Galin (1962)⁽⁸³⁾ attempted to establish a relationship between the lid flora and the disease. He found that massaging the lids often restored the normal flora; however, he did not really define the normal flora. In his thirty cases the following organisms were present: Staph aureus coagulase-positive, Alpha strep, Beta strep, Pneumococcus, Proteus, Pseudomonas, Budding yeast, and Staph.

Choyce, D. P.: (1964)⁽⁸⁴⁾ discussed the etiology of trachoma which is caused by a virus, but which often includes the effects of a superimposed bacterial infection which leads to difficulties in the treatment.

Many bacteria ordinarily associated with pathogenic processes may in some instances be members of the normal flora as is illustrated by the following articles.

"Leprosy is a chronic infectious disease affecting chiefly the skin, mucous membranes of the upper respiratory tract and certain peripheral nerves." (85) The prevailing opinion is that the bacilli entered the body through the injured skin and that in many individuals living in close association with known cases, the bacteria may thrive on the skin without resultant infection.

Two members of the panel "Problems in Diagnosis and Management of Gonorrhea" add salient points to the discussion since at times the gonococcus is at least a transient member of the flora.

"As regards gonorrhea, available information indicates that this disease is widespread, remains uncontrolled, and is now one of the most challenging health problems in many parts of the world. There are so many unreported cases of gonorrhea, that probably the incidence is ten or more times higher than actually is reported, and we may say that the reservoir of gonorrhea does not appear to have substantially reduced since the second World War." Many women and homosexual men spread gonorrhea without realizing they are infected and it is essentially a part of the normal flora of these people (86).

Catterall and Williamson (1963) (87) investigated the appearance of relatively insensitive strains of gonococci. They felt that this instance was related to the increasing frequencies of treatment failure in gonorrhoea following penicillin therapy.

It is necessary to consider the role that the transient flora may play in skin infection since in many specific instances the transient flora may become part of the normal flora of a particular individual.

deGrosz, I.: (1962) (88) has attempted to define the position of Mycoplasma hominis which is considered to be a potential pathogen as well as a symbiont. "The elucidation of the role of PPLO in the conjunctiva requires further research. The commensal nature of these organisms does not exclude their potential pathogenicity."

Additional evidence on the pathogenic character of PPLO has been supplied by Shepard, et al: (1965) (89) who have identified PPLO as being present in systemic lupus erythematosus and in Reiters' syndrome.

Whether a condition should be considered a disease when it is present in 20% of the normal population and is due to a bacterium closely allied to the normal flora has never been established. A recent study by Sarkany, I. et al: (1963)⁽⁹⁰⁾ has provided evidence of the bacterial nature of this disease (erythrasma). It was long thought to be due to the actinomycete, Nocardia minutissima, but these authors have given conclusive evidence that the etiological agent is Corynebacterium minutissimum. It affects the groin, the axilla and the toe web primarily.

This supports a study performed by Sarkany, I. et al: (1961)⁽⁹¹⁾ who found that 22 of 107 normal individuals had erythrasma. It was felt that the causative organism was a gram positive rod 1-2 μ by .3 to .6 μ , pleomorphic and gram negative in old cultures. It was a nonmotile and nonacid fast rod.

Acne

There is marked disagreement between authors regarding the possible factors indicted in the appearance of acne vulgaris.

In a recent study by English (1964)⁽⁹²⁾ three factors were felt to be responsible for the appearance of acne vulgaris in most patients. These include: (1) androgenic hormones, (2) follicular plugging, and (3) bacterial infection. They believe that antibiotics have a positive effect in acne due to their antibacterial properties. The specific bacteria indicted is a gram positive anaerobic diphtheroid which produces propionic acid from cebum. This bacteria has been termed "Propionebacteria, Corynebacterium acnes, or acne bacillus." The only pathogenic role this bacteria plays in the human is in the production of propionic acid from cebum. The bacteria are mainly present in those areas where the sebaceous gland is best developed; i. e., areas of the back, chest, face, and neck. The greatest concentration is in the sebaceous follicles and composes most of the plug in a comedo or whitehead. One can express literally thousands of these bacteria in a wormy extrusion from the side of an "adolescent nose".

Blau (1965)⁽⁹³⁾ whose study defined the resident bacteria on the face to include Staphylococcus albus and Corynebacterium acnes felt that these bacteria

inhabited the lesions of acne together, since they were seldom found alone. Eight percent of the blackheads contained a minor number of diphtheroids which also occurred in 3% of the pustules and 12% of the nodules. *Aerobacter* was found in 5% of the blackheads and E. coli in 3% of the pustules.

Kirschbaum, J.O., et al⁽⁹⁴⁾ was able to produce typical acne vulgaris by injecting Corynebacterium acnes into sterile sebaceous glands. This experimental demonstration of a normally harmless organism bringing about a rupture of a silent cyst may illuminate how inflammatory lesions arise in acne vulgaris.

Shehadeh, et al: (1963)⁽⁹⁵⁾ in a review of the microbiology of acne vulgaris felt that the exact role of bacteria in the production of acne has never been clearly defined. Authors are in disagreement as to the causative organism, Sabouraud* favored C. acnes, while Andrews, Becker and Cronk** felt that staphylococcus might be the causative organism. Bacteriological studies have also yielded virulent staphylococci, diphtheroids, and coliforms or completely sterile lesions. These authors⁽⁹⁵⁾ examined 60 patients and the dominant organism recovered in practically all instances was C. acnes. In addition, Staphylococcus albus was present in smaller numbers. In purulent lesions, Staphylococcus aureus and diphtheroids were recovered. In direct opposition to the work of Evans (1950), this author failed to recover anaerobic C. acnes except from cases of acne. This author⁽⁹⁵⁾ felt that the discrepancy was due to the fact that Evans had not transferred his cultures to aerobic conditions and found that the diphtheroids were in reality facultative.

A different approach was taken by Tanaka, et al: (1963)⁽⁹⁶⁾ who felt that acne vulgaris occurs in those areas where active sebaceous glands are densely distributed. The initial change in acne consist of elongation, dilatation and hyperkeratosis of the follicular neck due to the hyperfunction of the upper follicle. It is possible that there is, in addition, a hyperfunction of the sebaceous glands.

*Sabouraud

**Andrews, Becker and Cronk

The few references cited should point out the divergence of opinions on the etiology of acne vulgaris and it is felt that this particular review should not include an exhaustive study of acne, but rather highlight the role the "normal" skin flora seems to play in acne.

Protective Mechanisms

To adequately understand the shift from the normal flora to a frank infection, a thorough knowledge of environment, the physiology of the particular bacteria, the commensal possibilities, as well as individual resistance levels is necessary. In a paper given by Ericsson (1962)⁽⁹⁷⁾ these factors are so well summarized that many of the author's ideas are being quoted at length. "...the skin as a potential habitat for bacteria. The healthy skin for reasons which are not clearly understood, is highly unfavorable to bacterial growth. Some pathologic change in the function or morphology of the skin must be present if bacterial invasion is to succeed. This is true even when a microorganism, which from the purely bacteriologic viewpoint is to be regarded as highly virulent, is applied to the skin. Lesions which favor bacterial invasion are characteristic of eczema, juvenile seborrhea and burns, whereas other severe pathologic changes, for instances psoriasis, are remarkably unsuitable as a bacterial environment."

"The second ecologic problem is the mode of life of bacteria -- parasitic saprophytic or commensal where commensal means sharing the same food without interfering with each other. Typical commensal bacteria thus are normally present in the intestinal tract and the upper respiratory tract. Most skin bacteria are saprophytic and some few are parasitic. There is sometimes a tendency to exaggerate the pathogenic importance of bacteria, for instance of coagulase-negative staphylococci and corynebacteria in juvenile seborrhea, and to underestimate the importance of other bacteria, such as coagulase-positive staphylococci in burns. In healing burns we have found that even infections which from the clinical point of view look fairly superficial and harmless, nevertheless involve the whole immunity-producing system and therefore have a general effect on the body."

"The third ecologic problem in skin infections is the habits of bacteria. In this connection the sensitivity or resistance to antibiotics is of paramount importance."

'Summary

- (1) Prerequisites for skin infections are functional and/or anatomic disorders of the skin.
- (2) Elimination of these disorders is necessary for permanent cure of the infection.
- (3) Antibiotics only bring about a shift of the bacterial flora, but do not effect permanent cure.
- (4) The shift of the bacterial flora changes the clinical type of infection, sometimes to serious fulminant sepsis.
- (5) These factors have led to problems of hospital cross-infections in dermatologic wards. They motivate changes in the planning, equipment and staffing of dermatologic clinics." (97)

The skin displays an unusual ability to inhibit the growth of certain kinds of bacteria. Whether this is due to the resident bacterial flora or to certain anti-bacterial substances in the skin is a point of discussion between many authors. The work of Sprunt et al (1964)⁽⁹⁸⁾ is extremely interesting since it involved newborn babies whose skin flora theoretically should be non-existent. In this study the authors tried numerous in vitro experiments to determine whether vernix had any significant bactericidal activity against staphylococci or streptococci, but no conclusive results were reached. However, babies who were born with "no vernix" showed very high counts of staphylococci and seemed to acquire these high bacterial counts very rapidly.

Burtenshaw (1948)⁽⁹⁹⁾ wrote an interesting article on the self-sterilizing powers of the skin due to the presence of unsaturated fatty acids which have fungicidal and bactericidal powers. This is in agreement with Ricketts et al (1951)⁽¹⁰⁰⁾ who demonstrated the bacterial effects of fatty acids on pathogenic streptococci and staphylococci in vitro.

An excellent summary of protective mechanisms was written by H. Irvin Blank (1959)⁽¹⁰¹⁾ who considered the resident flora to consist of micrococci, diphtheroids, corynebacterium and propionibacteria and who felt that they did not cause disease as long as they remain on the surface, and that they may or may not be pathogenic, dependent upon the rate of reproduction. He felt that the mechanisms of protection are: (1) integrity of skin, (2) phagocytosis, (3) antibacterial substances,

and (4) formation and action of antibodies. Upon penetration, bacteria need not enter the capillaries, but can travel through the lymphatic system. In the lymphatic system a fibrin clot may act as a barrier mechanism.

The purpose of a study by O'Brien (1963)⁽¹⁰²⁾ was to gain evidence of modes of invasion of staphylococci and coliform bacilli. This was done by the application of a nutrient media to the skin which was selected for the organism concerned and strains of the respective bacteria were incubated in pure culture on the skin. The staphylococcal group of organisms invaded through the natural orifices of the skin; i.e., sweat pore, hair follicle. Once infection is established the staphylococci tend to localize. There is a multiplicity of lesions rather than a diffuseness. The lesions produced by E. coli showed many interesting differences. When they are incubated on the skin, an intense itching develops with a diffuse maculo-papular rash. Multiple vesicles formed in the epidermis which are not connected with the sweat ducts. These vesicles are then invaded by the bacteria. The bacilli actually seem to enter the skin at the point of an intense cell inflammatory congregation. Simply, it is a toxic vasculature followed by a bacterial invasion and the skin is no longer intact.

Among the many efforts which have been directed to determining the presence or absence of defense mechanisms in or on the human skin, is a recent study by Rothman, et al: (1963)⁽¹⁰³⁾. These authors listed the resident flora of the skin as Staphylococcus albus, diphtheroid lipophilic bacteria, Pityrosporon ovale and Propionibacterium acnes (in the grooves of skin folds and the canals of pilosebaceous apparatus). They listed the transient flora as hemolytic streptococci, Staphylococcus aureus, gram negative bacilli of fecal origin, and a variety of saprophytic bacteria. Enhanced susceptibility (agamaglobulinemia) was found to be a prominent cause of cutaneous pyrogenic infections. "Cutaneous resistance to viral attack may be based on classical immune mechanisms dependent on antibodies linked firmly to lymphoid cells." (103)

Scholtz, Jud R.:⁽¹⁰⁴⁾ studied the "chemical" barrier of the human skin and felt that the defense mechanism presented by the natural lipid surface film is extremely important particularly in the management of atopic dermatitis.

Burnett, J.W. (1963)⁽¹⁰⁵⁾ in a study designed to specify the pathogenic character of microorganisms found that "since the advent of antibiotic chemotherapy organisms regarded as normal flora in one part of the body have appeared as pathogens in other parts of the body with increasing frequency. One of the important problems in differential diagnosis facing the clinician today is the separation of pathogenic from nonpathogenic bacteria in a given infection." The following bacteria were viewed as potential pathogens: Listeria monocytogenes, Pasteurella multocida, Mima polymorpha, Chromobacteria, Salmonellae, Erysipelothrix, Bacteroides, Bacillus subtilis, and Alkaligenes fecalis.

In another study by S. Selwyn (1965)⁽¹⁰⁶⁾ of an endemic situation, the external skin lesions of in-patients were readily colonized by pathogenic bacteria present in the environment and a dynamic relationship existed between the bacterial flora. The bedding often yielded heavy cultures of prevalent pathogens, usually strains other than those of the bed occupant. Sixty percent of the hand cultures yielded pathogens. The incidence of Staphylococcus aureus was very high as well as that of gram-negative bacilli.

One hundred nine of 233 patients to whom anti-bacterial measures were not applied developed infected lesions after admission. Fifty-three percent of these were thought to be cross-infections, while 34% were superinfections. Fifteen cases, a small but significant group, were those in which autogenous infections occurred. Early recognition and elimination of clinical and subclinical infection in skin lesions is essential if gross environmental contamination is to be prevented.

One of the principal reasons for determining the normal flora of the skin is to define the role these organisms play in infection and disease, and the importance of environmental conditions upon the skin. It is also necessary to consider the effect of antibiotics on the normal skin flora, since if the equilibrium of the normal flora is upset either members of the normal flora or transient organisms can become predominant and overgrow. In addition the development of resistant strains is particularly important in the consideration of the staphylococci.

Physiological Factors

Localized physiological activity of bacteria has been studied by many authors from many viewpoints.

Rosebury⁽³⁾ states that "Host factors acting in skin against both indigenous and nonindigenous microbes have been reviewed by Rebell et al (1950), Marchionini and his co-workers (1928-39) presented evidence that alkalinity resulting from NH_3 production by bacteria in sweat favor proliferation of skin bacteria..." Additional information on the physiology of the human axillary apocrine sweat glands has been obtained by Shelly et al (1953)⁽²⁶⁾ who felt that the action of this localized bacterial population is a basic factor in the odors associated with sweat.

An interesting thesis study by Lizgunova, A. V. (1960)⁽¹⁰⁷⁾ has attempted to define the physiological protective function of the skin. A total of 499 specimens were taken from 373 humans and 545 cultures were investigated in detail. It was noted that the quantity of microorganisms per 1 sq. cm. of the skin depended on the age, living conditions, and occupation of the individual and ranged from 115 thousand to 32 million. The bactericidal properties of the skin varied according to the site. For example B. prodigiosus placed on the skin of the fingers died after 8 to 12 minutes; whereas on the skin of the back and forearms it survived 2-1/2 to 3 hours. Some strains of staphylococci which normally inhabit the skin surface were found in vitro to have protection properties enhancing the bactericidal function of the skin. The author⁽¹⁰⁷⁾ studied the protective powers of saprophytic microorganisms and the immunity reactions produced by the penetration of microorganisms into the skin of mice.

The shift from normal to pathological activity by ordinary cutaneous bacterial flora, as studied by Andrews et al (1963)⁽¹⁰⁸⁾, showed that this shift from normal to pathogenic activity of ordinary cutaneous bacterial flora is dramatic and may, in the presence of a minor dermatitis, suddenly be transformed so that normally harmless saprophytic staphylococcus, streptococcus, or Candida albicans assume a pathogenic role and cover the body surface. This was demonstrated by culture, intradermal, and patch tests. There is a rapid response of these eczematous eruptions to the proper antibacterial and antimycotic remedies.

Miles, A.A. (1955)⁽¹⁰⁹⁾ found that there was a marked difference in the resistance to bacterial infection which was dependent upon the route of entry of the bacteria; i.e., after intravenous injections the tolerance was higher than after subcutaneous injections.

Whether the inhibitory powers of the skin exist and, if so, what they are and against what are they effective has been studied by Hill et al (1933)⁽¹¹⁰⁾ who performed 1,444 tests using 12 strains of bacteria in a series of six subjects. The skin inhibited the growth of bacteria in 199 cases or 13.7%. Its action was most marked on gram positive spore-forming bacilli and less on the staphylococci and gram negative bacilli testing. Individual inhibitory action varies from 5.4% to 27.9%.

In a more recent study Scheiman et al (1960)⁽¹¹¹⁾ studied the effects of sterilization of skin surfaces and felt that this sterilization suppressed the skin's natural lipolytic activity. In addition they felt that probably surface bacteria participate in the formation of free-fatty acids on the surface, and considering the fungistatic and bacteriostatic effects of some of these free fatty acids that one might regard bacterial origin of free fatty acids a new example of ecological equilibrium in bacterial flora. Some bacterial species produced substances which keep other bacterial and fungal species in check.

In a different approach to the bactericidal activity present in the skin Buharin, O.V.: (Oct. 1962)⁽¹¹²⁾ concluded that Vitamin B₁₂ is a major factor in increasing bactericidal activity in diseases of the skin.

Arnold, L. (1930)⁽¹¹³⁾ defines the self-disinfecting power of the body surfaces as the ability to destroy exogenous bacterial life. The one function common to all body covering layers is the ability to control endogenous bacterial flora growing on them. There is an obligate microbic flora upon various body areas which is relatively constant, and the exogenous strains seem to be destroyed. The author performed experiments using various strains of bacteria both on living skin and the skin of cadavers. His conclusion was that living skin did have an inhibitory effect upon the growth of bacterial cultures. He also investigated strains of

Staphylococcus albicans from several body areas in an effort to determine whether there was a difference in the varying skin strains. Two hundred twenty-five strains obtained from under the fingernails did not show the same biological activity as strains from other skin areas. These strains were deficient in lactose fermentation. A particularly apt quotation from Rebell, G. (1959)⁽¹¹⁴⁾ follows: 'It may safely be assumed that whenever in nature two or more species of microorganisms grow in intimate association, each will interact with the other, and if, as in the present instance, the microorganisms grow upon the host organism then the host will be influenced by the interactions. "⁽¹¹⁴⁾

The production of antibacterial substances by other bacteria as discussed by Rosebury⁽³⁾ has certain pertinent highlights. For example, in a paper by Su, T. L. *, micrococcin is discussed and its bacteriostatic effect against Bacillus subtilis, staphylococci, streptococci, Str. faecalis, Corynebacterium diphtheria, B. anthracis and streptomyces. In papers by Heatley, et al ** and Halbert, et al *** staphylococcus cultures obtained from patients with conjunctivitis were studied and the authors found 9 different antibiotic agents which acted significantly only against gram-positive Corynebacteria hofmanni, Sarcina lutea, Mycobacterium smegmatis, streptococci other than enterococci, Bacillus species, clostridia, and staphylococci. In a study of 500 skin staphylococci by Lizgunova, A. V. **** 50 strains were found, including both albus and aureus strains, that inhibited the range of Enterobacteriaceae and both hemolytic and non-hemolytic streptococcus.

* Su, T. L.: (1948b), Ibid, vol. 29, pp. 473.

** Heatley, N. G.; Kelly, B. K.; and Smith, N.: 1952, J. Gen. Microbiol., vol. 6, pp. 30.

*** Halbert, S. P.; Swick, L. S.; and Sonn, C.: 1953, J. Immunol., vol. 70, pp. 400.

**** Lizgunova, A. V.: 1958, J. Microbiol. Epidemiol., vol. 29, pp. 297.

The inhibitory activity of cultures of Staphylococcus aureus against corynebacteria were established by Parker, et al^{*} who found that one-half of the cultures of Staphylococcus aureus recovered from impetigo inhibited corynebacteria.

A specific example of the bactericidal effect of certain substances formed by bacteria is highlighted by Hellerstrom, Sven⁽¹¹⁵⁾ in a discussion of Problems in Diagnosis and Management of Gonorrhea. "Sometimes, the mixed bacterial flora on the mucous membranes, particularly in women, is a serious problem. It may, for instance, be gonococci and staphylococci which latter bacteria can form a substance, penicillinase which renders the effect of the penicillin inactive." ⁽¹¹⁵⁾

In an article by Miyakawa, M. (1959)⁽¹¹⁶⁾ the interesting result of these germ free animal studies seems to indicate that the normal flora contributes to the healing process by inhibiting the epidermal layer reconstitution and hence establishing the inner-outer sequence of healing.

Compound infections are the rule rather than the exception in many dermatoses and the course of the disease is never simple. One of the outstanding discussions of compound dermatoses is by Tumarkin, B.M. (1960)⁽¹¹⁷⁾ who in a study of 70 patients noted the development of the staphylodermitis in 68 which coincided with the rapid improvement of the main dermatosis (chronic eczema or progressive psoriasis). The improvement of the main dermatosis, due to a fall of the allergic reactions of the organism, is connected with a depression of the immunological processes while the state of increased reactivity gives way to a state of increased susceptibility.

In addition to the influence of those substances produced by the normal flora and those applied knowingly by man to his skin, marked influences are generated

* Parker, M.T.; Tomlinson, A.J.H.; and Williams, R.E.O.: 1955, J. Hyg., vol. 53, pp. 458.

by environmental conditions and as stated by Marshall (1964)⁽¹¹⁸⁾ "Race, climate, nutrition and way of life are also contributory to the incidence of skin disease."

Few reports have been based on genetic incidence of skin disease. An outstanding report is that of Newhouse, Muriel L. (1964)⁽¹¹⁹⁾ who studied a series of Europeans and found that the occurrence of skin diseases was inversely related to the degree of pigmentation of the group. Statistically significant 5% level of confidence was reached. In a survey of 1,233 workers, acne vulgaris was present in 8.2%, tinea pedis in 7.4%, psoriasis in 4.1%, warts in 4.1% and lichen planus in 0.8%.

In another large series of patients (2,000) El Zawahry, M.⁽¹²⁰⁾ found that skin diseases due to bacteria and caused by infection were 653 and 32.65% of the dermatoses were due to infection, usually fungi; i. e., ringworm of the scalp.

In a localized effort to determine the causative factor of nail disease White et al (1963)⁽¹²¹⁾ studied microscopically 1,252 cases of diseases of the nail. Five hundred eighty-nine were due to ringworm, 44 were due to Candida albicans, and 113 were due to mixed fungus and bacteria, 81 were due to staphylococci, and 2 were due to lepra bacilli.

A factor in individual susceptibility is the immunoresponse to a particular bacterial strain as explained by Ouchterlony, Orjan (1963)⁽¹²²⁾ "Immunodiffusion analyses can sometimes help us to determine the immunoresponse in individuals exposed to infections, particularly if the infections are repeated or of a chronic type." (122)

Rostenberg, Jr., Adolph (1965)⁽¹²³⁾ dealt with allergic sensitization and felt that the delayed sensitization would include bacterial as well as eczematous and homograph agents.

Marked hypersensitivity as a function of immunoresponse is discussed by Millman, Milton (1964)⁽¹²⁴⁾. A symmetrical eruption on the palms or soles, or both, of tiny vesicles and sterile pustules may result from distant skin infections similar to "id" reactions of trichophyton. In addition, there is a marked

hypersensitiveness to certain bacterial substances such as the Bacillus tuberculosis. The author discusses the use of staphylococcus toxoids or autogenous vaccines in the treatment of furuncles and carbuncles.

In any consideration of immunology and allergy, particularly those due to a bacterial source, certain basic questions are raised as summarized by Miescher, P. et al (1963)⁽¹²⁵⁾.

- "(1) Do skin specific antigens really exist, and if so, what is their chemical nature?
- (2) Do autoimmune skin reactions occur in human disease due to antibody and/or delayed type of hypersensitivity?
- (3) Are such autoimmune reactions pathogenic for the organism?
- (4) Can the skin be the site of autoimmune reaction involving autologous antigens derived from other organs?"⁽¹²⁵⁾

A study by Maibach, H. (1963)⁽¹²⁶⁾ attempted to examine a large number of individuals to determine the effectiveness of Staphylococcus toxoids. "The great natural variability of rates of infection at different times of the year necessitates the simultaneous treatment of both patients and controls." Three hundred individuals were sampled. One hundred fifty were a control group and 150 were divided into groups receiving immunizations. "There were essentially the same number of total infections in each group whether one compares the number of individuals with one infection, two to four infections or five or more infections. Again, these differences are not statistically significant." "We think that it can be clearly stated that the vaccines used in this study had very little effect on either the number of individuals infected or the number of lesions in a given patient."⁽¹²⁶⁾

In an investigation of the biology of the human sebaceous gland Kligman, et al (1958)⁽¹²⁷⁾ made the following observations: The physical state of sebum is important in maintaining flexibility of the skin. The integrity of the skin is highly important in preventing microbial infection. "The chemical nature of sebum is of still greater importance in the ecology of the skin, since certain of its constituents have been shown to be inhibitory to the growth of a number of potentially pathogenically pathogenic microorganisms."⁽¹²⁷⁾ There is also

evidence that Pityrosporum ovale are able to utilize sebaceous products. The fatty acids play a significant part in determining the pattern of life on the skin. They appear to be a by-product of metabolism of lipolytic organisms. It is reasonable to assume that propionibacterium is responsible. It is also significant that this bacterial species can utilize sebum as a nutrient. This information is in agreement with that obtained by Strauss et al⁽¹²⁸⁾.

Marples, M. (1965)⁽⁶⁾ has discussed extensively the nutrients in the skin as a prime factor in the ecology of the skin. She felt that the surface of the skin has an oily mixture dispersed in a weak saline solution. The surface is bathed with a dilute solution of electrolytes. Part of the nitrogenous material on the surface of the skin is locked-up in fragmentating keratin (only dermatophytes can utilize this material). She considers only the soluble nitrogenous substances as contributing to the nutrition of the skin population. Rothman in 1954 showed that substances can be dissolved in the eccrine sweat or can be formed as soluble by-products of keratinisation reaching the surface by the transepidermal route.

The nitrogen present on the skin is dependent upon the environment, i.e., if the protein intake is 98 grams per day the nitrogen dermal loss is 15 milligrams in a comfortable environment but 152 milligrams in a hot and humid environment. The nitrogen is available as urea and as amino acids. Extensive work on the amino acids has been done by Flesh, P. (1958)⁽¹²⁹⁾ who felt that the free amino acids were important as water binders in regulating the trans-epidermal flow of water.

The proportion of amino acids in sweat in contrast to those in blood plasma were determined by Hier, S.W. (1946)⁽¹³⁰⁾. A specific study was done by Silva, M. (1958)⁽¹³¹⁾ who studied the stimulatory and inhibitory effects of amino acids identified on the skin against varying strains of bacteria in vitro.

Chiang, S.P. et al (1955)⁽¹³²⁾ determined the protein fraction of the normal cerumen and found that this protein fraction includes the debris of the skin, hair, and bacteria and accounts for 25% of the fraction. The lipid fraction is from 40-50% and 20% of the cerumen is non-lipid protein material. The size of this fraction may

be dependent upon the freshness of the sample and is a product of metabolic activity.

The neutral proteolytic activity of the human epidermis in normal and pathological conditions was studied by Finzi, A. (1963)⁽¹³³⁾ who stated "With this research, the total (endo- and exopeptidasic) neutral proteolytic activity of human epidermis was studied for the first time, under the most physiologic conditions, i.e., without enzymatic extractions, which are always incomplete and denaturing, and using the optimum substratum, the proteins of the epidermis. The results obtained in patients with psoriasis do not agree with recent findings which attribute a pathogenetic importance to the decrease of the amino acids and polypeptides of the skin, due to reduction of local proteolytic activity. The results reported by others may depend on the non-uniformity of the material examined (e.g. whole skin, scales only, etc.). It is obviously difficult to determine quantitatively the percentage of ortho- and parakeratotic products present in the tissues studied -- products which, being almost completely devoid of metabolic activities, are obviously also low in enzymatic activities. "

The study of Rockl, H. et al (1959)⁽¹³⁴⁾ considered the quantitative distribution and depth of the normal microbes of the skin in the stratum corneum as well as the microbial distribution in the excretory ducts of the sweat and sebaceous glands of the skin. They used the "Tesafilm tear" method to obtain the specimens. The sweat and sebaceous fluids were carefully extracted. About 75% of the bacteria were found between the hornlamella of the "Pars disconjuncta" and the remaining 25% in the "Para conjuncta". These authors did not find any microbes in the sweat and sebaceous glands and their excretory ducts which is in direct contrast to the work of many authors, but is supported by the work of Lovell, D. L. (1945)⁽¹³⁵⁾ who found in a determination of the resident flora of the sebaceous glands that all bacteria were in reality outside the body and none were seen in or between living cells. They considered the resident flora to be Staphylococcus albus and Staphylococcus citreus and transient flora could be composed of any microorganisms.

The possibility that the sympathetic system is involved in the ecology of the skin was investigated by Balenska et al (1964)⁽¹³⁶⁾ who examined the condition of the

receptor function of the skin in 48 patients with boils. Changes were recorded in the excitability of the skin reaction with a tendency toward an increased excitability. Hyper reaction of the sympathetic system seemed to accompany the skin infection.

In an effort to elucidate the parameter defined as penetrability or permeability, a study by Monash (1957)⁽¹³⁷⁾ used typical anesthetics, antihistamines and histamines to establish the exact location of the barrier to skin penetration. He found by the removal of the outer half of the stratum corneum they increased the skin penetrability markedly.

Influence of Physical Factors

In civilized countries many areas of the body are frequently submitted to the application of soap and water and its effect upon the indigenous flora has been defined by many authors. An excellent study by Miedler, Leo J. et al (1960)⁽¹³⁸⁾ dealt with subjects who were male medical students or members of the hospital staff. They used antiflora detergent or soap bar exclusively. They were examined initially, at four, and at eight weeks. Thirty-nine of the 60 volunteers had mycotic infections. The mycological activities were not particularly marked for anaflora. In the bacteriological studies made from the foreheads of the subjects, coagulase positive staphylococci were isolated initially from three subjects, but not on subsequent culturing. However, the coagulase-negative staphylococci increased markedly at subsequent cultural periods. Hemolytic streptococci were isolated from 9 subjects initially, but dropped by 60% in subsequent cultures. Non-hemolytic streptococci remained constant. The authors' conclusions: anaflora is more active against potential pathogens than against non-pathogenic bacteria.

Another study of the effects of soaps on the skin was performed by Bettley (1960)⁽¹³⁹⁾ who felt the skin of the face is a poorly colonized habitat probably due to the effect of soap and water. However, the sebaceous glands may become enlarged and become invaded by *Demodex folliculorum*. Also, lesions of *Tinea corporis* due to *M. canis* is more likely to occur on the face than elsewhere. In males the bearded area is vulnerable to infection and sycosis barbae as a result

of invasion either by fungal or bacterial pathogens is probably the result of the trauma of shaving. Also, in sunburn you may expect extensive lesions of Herpes simplex.

The customs of society in many areas of the world today require the application of deodorants to the axilla and a study of the effect of these Topical Antibacterial Agents on the Bacterial Flora of the Axilla was performed by Kligman (1963)⁽¹⁴⁰⁾. These authors⁽¹⁴⁰⁾ felt that it was important to determine the effect of the topical application of antibacterial substances on the resident microflora of the axilla. Dominant resident flora were coagulase-negative staphylococci, diphtheroids, Aerobacter species and alkaligenes, Staphylococcus aureus appeared transiently. It is particularly important to realize the inherent danger of fungal invasion following topical applications.

An extraneous factor which may or may not influence the normal flora of the skin is ultraviolet light. The article by Lorincz, A. (1960)⁽¹⁴¹⁾ establishes the physiological effects of ultraviolet light upon the skin and establishes an acquired tolerance to sunshine subsequent to repeated exposures due to two mechanisms -- increased melanin pigmentation and thickening of the horny layer. Sweat also affords some protection of the skin against sunburn. In animal research it was found that marked blood changes followed ultraviolet irradiation including an increase in the histamine content of the blood, a decrease in the serum cholesterol, and a flattening of the glucose tolerance curve as well as a decrease in serum tryosine. No mention was made of the effect of ultraviolet upon the bacterial flora of the skin.

In contrast the influence of ultraviolet light on post-operative infections was discussed at length in an editorial in JAMA (1964)⁽¹⁴²⁾. Five universities and medical centers installed ultraviolet lamps in operating rooms, adhered to a double blind random treatment protocol and recorded observations for 27 months. Two thousand two hundred nineteen plates showed a mean colony count reduction of 56.3% in the use of ultraviolet lamps. There was a statistically significant result in the rate of the post-operative infection drop from 3.8% to 2.9% in those patients operated on under ultraviolet lamp conditions. The interesting side

result was that infections occurred more frequently in irradiated wounds than in non-irradiated wounds, although irradiation reduced the risk 25%.

The effect of temperature upon the skin flora has been ill defined. One of the few articles considering the importance of this factor is by Hertzman, A.B. (1953)⁽¹⁴³⁾ who believed that temperature may well be the localizing factor in the invasion of the foot by the dermatophytic species. Bacteria on the legs and the feet must be able to withstand marked fluctuation in temperature.

Important both in the physiology of the flora and of the skin is pH since it will determine the extent of growth or the limitation of growth of many bacterial specimens. In a study, Beare, et al (1956)⁽¹⁴⁴⁾ determined the acid base balance of the skin. The pH of the skin surface of children with seborrheic dermatitis was compared with unaffected children. They found that the pH of much of the skin was 5.0, but that in the inguinal area the pH of skin approached neutrality due to the specialized character of the skin in the inguinal area.

Additional work on pH as related to the human ear canal was performed by Shelley, et al (1956)⁽¹⁴⁵⁾ who found that freshly secreted cerumen has a pH of 5.0 to 5.5 and its change towards alkalinity is part of a biological process.

One of the basic requirements for bacterial growth is the presence of moisture in sufficient quantities to encourage reproduction. In a basic study performed by Blank et al (1958)⁽¹⁴⁶⁾ the effect of moisture content of sheets of callus on the growth of various microorganisms was determined.

Table 29

EFFECT OF MOISTURE

<u>"Organism</u>	<u>Prevents Growth</u>	<u>Allows Growth</u>
<u>M. pyogenes</u>	23	29
Micrococci	23	29
Coliform bacillus	36	50
Diphtheroids	50	70 "

That "few if any bacteria can successfully penetrate the normal cornified epithelium" Hughes, W.H. (1948)⁽¹⁴⁷⁾ is a well known fact and for this reason the

establishment of the water lipid coefficient was felt to be necessary by Clendenning et al (1962)⁽¹⁴⁸⁾ who performed in vitro tests of skin taken from breasts and legs in order to determine the penetration of the superficial epidermal barrier by weak non-electrolytes. Consideration was given to molecular size, viscosity, hydration, temperature and period of contact.

Of particular importance in any consideration of space travel is the effect of abnormal atmospheres upon the indigenous microflora of man. An excellent study has been performed by McAllister (1963)⁽¹⁴⁹⁾ on the inhibitory effects of hyperbaric oxygen upon bacteria and fungi.

The effects of oxygen at increased pressures in the treatment of anaerobic infections is well known, but little attention has been directed to the effects of hyperbaric oxygen on aerobic microorganisms. Different microorganisms vary in their susceptibility to increased O₂ tension with Pseudomonas pyogenes, Staphylococcus aureus, E. coli, Candida albus, and Aspergillus fumigatus being most affected. "The basic effect of hyperbaric oxygen appears to be inhibitory rather than cidal. Pseudomonas pyocyanea, Staph aureus, E. coli appeared to be permanently altered by their exposure to hyperbaric oxygen and they failed to attain the appearance of the controls. Staph aureus after 42 hours exposure continued to grow but as stunted non-pigmented colonies but they were slide-coagulase positive. A few colonies (well separated) were larger, atypical and hyperpigmented - 'Hyperbars'". "...there seemed to be no dramatic-alteration in the antibiotic sensitivity." "It is essential to know the oxygen tensions at which individual bacterial species might be stimulated or inhibited, and growth/oxygen-pressure curves for each should be drawn to avoid alteration of normal body flora or the differential stimulation of pathogens in infection." (149)

In a more recent study Ross et al (1965)⁽¹⁵⁰⁾ studied the possible protective action of hyperbaric oxygen in mice with pneumococcal septicaemia and found that exposure to oxygen at 2-3 atmospheres markedly inhibited the growth of some aerobic and obligatory anaerobic bacteria as well as changing their colonial morphology. It was found that hyperbaric oxygen could alter the course of an aerobic septicaemia and can by its antibacterial activity significantly prolong the survival

of the infected host in pneumococcal septicaemia. The author felt that infections, by the following sensitive aerobic bacteria, Staph aureus, E. coli, Pseudomonas pyocyanea and Streptococcus veridans might be amenable to treatment with hyperbaric oxygen either alone or in combination with conventional antibiotics providing that the bacteria are in situations where the antibacterial oxygen tensions are readily available such as the skin.

RECOMMENDATIONS

The importance of devising standard sampling techniques cannot be overstressed since many of the discrepancies in the literature are the direct result of the varying sampling techniques. Studies evaluating the varying collection methods such as those of Price⁽¹⁾ who cultured the rinse following a surgical scrub, Evans⁽⁴⁾ who used a scraping technique, Pillsbury⁽¹²⁾ who devised a rotating brush technique for collection, Updegraff⁽¹⁰⁾ who standardized the Scotch Tape stripping technique, and Gorrill⁽¹⁵¹⁾ who used a velvet replicating plate technique should be undertaken.

Of equal importance are the procedures used for the culturing of the samples. Proper media, including both aerobic and anaerobic, are essential and, in addition, the OR potential of the media should be determined. In specific instances, special nutrients must be included in the media to insure the recovery of all bacteria present in the sample. A study of the OR potential of medias which are used to recover the Corynebacter species from the skin are particularly needed to clarify the position C. acnes plays in the normal flora of the skin. In addition, any study of the scalp flora should include media supplying the oil requirement of P. ovale.

The importance of studying bacteria in the particular microbial community which they inhabit cannot be overstressed since no in vitro study of single cultures can possibly elucidate the interactions between varying microbial species or even intraspecies reactions. Cooperative and competitive interactions should be defined. In vitro studies may contribute to an understanding of the factors leading to homeostasis.

The host-parasite relationship as portrayed in the ecology of the dermal microflora illustrates the fact that the pathogen must compete with the normal flora for nutrients and space to establish his colony. The delicate balance of the normal flora when disturbed by the application of topical materials, particularly antibiotics or corticosteroids, may be completely upset since microbial members of the flora that hold pathogens in check may be wiped out, allowing the pathogens

or other members of the flora to appear in large numbers with possible undesirable effects; i. e., fungal takeovers are hard to cope with, since only one antifungal agent is particularly effective.

Another area requiring more study is the mode of spread or invasion of the skin by undesirable members of the biocenosis. This is particularly important in hospitals where cross-contamination is a severe problem as in burn cases or in dermatological wards.

Among factors requiring more investigation is the determination of the probable seasonal rhythm associated with skin microflora. This may be a factor resulting from the drying of the skin in the winter, since higher bacterial counts are associated with oily skin and those areas where perspiration is excessive. This study should investigate seasonal variation in concentrations of lipids and moisture of different body skin areas. In addition to the effect of the seasons and humidity on the skin flora, the zenith distance of the sun, the altitude, the ozone in the atmosphere, the degree of pigmentation of the host, habits of his dress or undress are all important factors determining climatic influence on flora.

The role that pure oxygen environment at reduced pressure plays in the physiology of the aerobic bacteria has not been defined. Studies involving the hyperbaric use of oxygen have shown changes in colony formation and physiological patterns of bacteria that seem to point out the necessity for in vitro studies to elucidate the role that 100% O₂ at reduced pressure may play in the potential pathogenicity of the normal flora.

In addition, the role that radical changes in temperature and/or humidity play in the stability or instability of the normal flora has not been clarified and should be studied. In a recent Republic Aviation study the fluctuation of total skin counts may have been a reflection of the extreme variations in humidity.

The host-parasite relationship is an interactive balanced ecology, with not only competitive but cooperative modes of life, established on the skin. A thorough

understanding of the delicate balance necessary to maintain a "normal" situation is necessary to evaluate those shifts in the normal flora caused by the use of antibiotics, adverse environmental conditions, allergic sensitivity, or a radical change in personal hygiene procedures. It is necessary to study the dynamic equilibrium of the microflora and to clarify the part the intrinsic and extrinsic factors play in this equilibrium.

The literature seems to reflect that insufficient research has been performed to establish sufficient knowledge of the kind and significance of host defense mechanisms against bacterial contamination and the relationship of the degree of contamination to the severity of the bacterial invasion. This knowledge is necessary to evaluate many modes of medical treatment.

A study of bacterial inhibition phenomena should be undertaken in order to determine whether this is due to antibiotic substances produced by the effector species; and consider the possibility of using different species of bacteria to limit frank infections which do not respond to antibiotics, in much the same way that staphylococci implantation has been effective in the limitation of certain hospital epidemics of staphylococci in newborn nurseries.

It is difficult to find statistics concerning the incidence of many common skin infections. It is possible that symptomatology may be completely absent in many people and for this reason it is difficult to determine the actual incidence. In addition, little has been done to determine the effect of specific disease on the normal inhabitants of the skin or the effect of the inhabitants on the specific disease.

In many recorded cases, shifts of bacterial flora change the clinical type of infection, sometimes to a serious fulminating sepsis. It is important to remember that prerequisites of skin infection are functional or anatomical disorders of the skin.

The epidemiology of cutaneous disease is being studied and it is hoped future research will clarify the methodology of the evaluation of factors such as race, geography, and personal habits upon endemology. These studies should include sufficient data to evaluate the age and sex incidence of specific cutaneous diseases.

The necessity for establishing criteria determining the microbial compatibility of men who will be living in close proximity for long periods of time in a "closed" community is essential. For example, Staphylococcus aureus is a predominant organism in the nares of many individuals, and is an essential member of the balanced flora of these individuals; however, individuals who do not carry this strain would be particularly susceptible in a "closed" environment and "natural" defense mechanisms against continual exposure to large quantities of microorganisms might not be sufficient to maintain health.

The identification of varying strain types of the indigenous gram-positive rods and cocci is extremely difficult since no identification schema exists. As many as 56 strains of corynebacter or unidentified gram-positive rods have been recovered from one body area. There has been no classification developed (similar to the work done by Kaufman and White on the gram-negative rods) and this research area requires immediate emphasis. This is necessary, not only from the viewpoint of identification and classification, but to determine the actual role this large group of predominating organisms assumes in the microbiota. More work is currently being done on the gram-positive cocci in order to differentiate the staphylococci from the micrococci, but wide areas of research remain in this segment of the bacterial flora.

The most important studies which should be undertaken immediately are:

- (1) Clarification of the host-parasite relationship.
- (2) Microbial compatibility between hosts.
- (3) Effect of atmospheres peculiar to space flight on normal flora in vitro.
- (4) Development of identification schema for gram-positive rods.
- (5) Standardization of sampling techniques for skin studies.
- (6) Definition of nutritional requirements of all species, both aerobic and anaerobic, present on the skin.

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